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VIRTUAL LAF CONFERENCE

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SUBJECT: LAF & ACE Inhibitors

Erling suggested that a discussion of the possible role of angiotensin converting enzyme inhibitors (ACE inhibitors) in afib might be a worthy subject for discussion in the Conference Room. I wholeheartedly agree. To bring everybody up to speed I have posted below an excerpt on the subject from the March 2003 issue of The AFIB Report. Although it emphasizes the role of aldosterone in fibrosis it also discusses some recent findings regarding ACE inhibitors such as enalapril as well as a possible role for angiotensin II receptor blockers in managing LAF.

Please join the discussion!

"Aldosterone is known to have many detrimental effects on the heart and some of them are associated with conditions known to promote LAF:

· Inflammation and fibrosis of the heart tissue are found in most LAF patients. Aldosterone causes inflammation and fibrosis of the heart tissue by direct action on the MC-receptors in the myocardium. This action is not accompanied by hypertension.

· Most LAF patients suffer from a systemic inflammation as expressed in abnormally high CRP (C-reactive protein) levels. Aldosterone causes inflammation.

· Atrial fibrillation is associated with an increased level of reactive oxygen species (ROS) in the heart tissue. Aldosterone causes an increased level.

· Atrial fibrillation is associated with an imbalance in the ANS. Aldosterone causes such an imbalance, primarily by increasing sympathetic activity.

· Hypokalemia (low potassium levels) is associated with an increase in PACs, which in turn are associated with an increased risk of LAF episodes. Aldosterone promotes hypokalemia.

· Hypomagnesemia (low magnesium levels) is associated with an increase in PACs, which in turn are associated with an increased risk of LAF episodes. Aldosterone promotes hypomagnesemia.

Although aldosterone production is primarily initiated by activation of the RAAS, it can also be initiated by ACTH the same hormone that stimulates the secretion of cortisol. A high potassium level or a low sodium level also causes aldosterone secretion to be increased. A magnesium deficiency causes an increase in aldosterone production and subsequent hypokalemia (potassium deficiency). An excess of calcium ions (Ca++) can also increase aldosterone production because excess Ca++ increases the secretion of ACTH.

An excessive production of aldosterone can also be caused by a benign tumour (adenoma) on the adrenal glands or

simply by an enlargement (hyperplasia) of the adrenal glands. Hyperplasia itself has been linked to prolonged exposure to stress. Adrenal tumours are fairly common and can be genetically “ordained”.

As mentioned previously, aldosterone production is primarily initiated by the renin-angiotensin-aldosterone system. The RAAS is the body’s main system for dealing with a decrease in blood pressure that is too great to be handled by the autonomic nervous system alone. The primary purpose of the RAAS is thus to increase blood pressure by preserving (hoarding) sodium and water. The RAAS is normally activated by hypotension caused, for example, by a sudden shift from supine to standing position. The low blood pressure is first sensed by the kidneys, which proceed to secrete a small peptide called renin. Renin is transported to the liver where it helps to produce angiotensin I from a large protein called angiotensinogen. Angiotensin I, in turn, is carried by the blood to the lungs where it is converted into angiotensin II through the action of angiotensin-converting enzyme (ACE).

Angiotensin II is the most potent vasoconstrictor in the body. It causes the blood vessels to constrict and potentiates the sympathetic nervous system resulting in an increase in blood pressure. Angiotensin II also acts on the adrenal glands to produce aldosterone. Aldosterone causes sodium and water to be retained by the kidneys thus increasing the body’s fluid content and thereby the blood pressure. The action of the renin-angiotensin part of the RAAS may take seconds to minutes to kick in, but it may take days or even weeks before the full effect of aldosterone is felt.

If there is little medical evidence at the moment that aldosterone is involved in afib, is there any evidence that other parts of the RAAS may be? Indeed there is.

Researchers at the University of Leipzig in Germany recently reported that lone afibbers have significantly more receptors for angiotensin II (subtype I) in the left atrium than do people without LAF. The increase in receptors was apparent in both afibbers with mitral valve prolapse and in those without it. No increase in receptors was found in the right atrium. The researchers conclude that angiotensin II receptor subtype I may play a role in lone atrial fibrillation[1]. The presence of more receptors in afibbers would mean that the level of whatever protein is produced as a result of the angiotensin II molecule docking at its receptor would be elevated. If this protein, or perhaps aldosterone itself, is involved in promoting afib then blocking the subtype I angiotensin II receptor should result in a decrease in afib episodes.

Angiotensin II type 1 receptor (AT1R) antagonists are potent blockers of the receptors. Japanese researchers have found that candesartan (Atacand) significantly shortens afib episodes in dogs and prevents structural remodelling and fibrosis in the atrium[2]. Spanish researchers have found that the AT1R irebesartan (Avapro) allowed afibbers with persistent afib who were electrically cardioverted to stay in sinus rhythm longer after treatment with irebesartan + amiodarone than did patients medicated with amiodarone alone[3].

There is evidence that the AT1R valsartan (Diovan) can actually reduce aldosterone levels. A team of American and Italian researchers treated over 4,000 chronic heart failure patients with valsartan (160 mg twice daily) or placebo and compared plasma aldosterone levels after 24 months. The mean aldosterone level in the placebo group increased by 18.8 pg/mL, but decreased by 23.8 pg/mL in the valsartan group. Thus the mean reduction in aldosterone in the valsartan group compared with the placebo group was 29.3%. The difference between the two groups was most pronounced after just 4 months of treatment[4]. The same group of researchers later concluded that the incidence of new cases of atrial fibrillation among the heart failure patients was significantly lower in the valsartan group than in the placebo group (5.27% versus 7.86% in 23 months of follow-up)[5].

Chinese researchers have found that the AT1R losartan (Cozaar) actually inhibits the production of aldosterone in the myocardium of rats with heart failure[6].

An alternative way of preventing the detrimental effects of angiotensin II is by inhibiting its synthesis as opposed to blocking its uptake (with AT1Rs). Angiotensin-converting enzyme inhibitors (ACE inhibitors) prevent the synthesis of angiotensin II from angiotensin I. There is now some evidence that ACE inhibitors may indeed affect afib episode frequency. Taiwanese researchers recently reported that the ACE inhibitor enalapril (Vasotec) significantly lengthens the afib-free interval following electrical cardioversion of chronic afib when given in combination with amiodarone. After 270 days 74% of the amiodarone + enalapril group was still in sinus rhythm as compared to only 57% in the amiodarone only group[7].

Danish researchers have found that the ACE inhibitor trandolapril (Mavik) decreased the risk of developing atrial fibrillation by over 50% in a group of heart disease patients (left ventricular dysfunction) who had just suffered a heart attack[8]. They point out that ACE inhibition is associated with a reduction in atrial premature beats (PACs), the forerunners of atrial fibrillation, and also tends to prevent enlargement of the left atrium.

Conclusion

Evidence is slowly accumulating to the effect that the RAAS or, perhaps more specifically, angiotensin II and aldosterone may indeed be involved in atrial fibrillation. There is now also emerging evidence that ACE inhibitors and angiotensin II receptor antagonists may act to prevent atrial fibrillation episodes most likely through a reduction in PAC frequency and prevention of structural and electrical remodelling of the atrium. Most research, so far, has involved patients with heart failure or other heart disease, so it is not clear whether the findings are applicable to lone afibbers. However, the observation by the University of Leipzig team that lone afibbers have an abnormally high level of angiotensin II type 1 receptors in the left atrium certainly lends support to the idea that the RAAS is involved in lone afib as well. If this is indeed so then ACE inhibitors or angiotensin II receptor antagonists may prove to be of some benefit in the treatment of LAF, particularly among afibbers with high blood pressure. Both types of drugs, of course, have many undesirable side effects and there are also indications that the effect of some of them, particularly the angiotensin II receptor antagonists may wear off over time[9,10].

The potential benefits of drugs that block aldosterone (mineralo corticoid) receptors rather than angiotensin II receptors should not be overlooked. Spironolactone, a potassium-sparing diuretic, is highly effective in blocking MC-receptors. By doing so, it rebalances the autonomic nervous system (increases parasympathetic activity and decreases sympathetic activity), decreases the risk of stroke, prevents hypokalemia, reduces fibrosis, improves endothelial function, and helps prevent hypertension (by blocking MC-receptors in the brain).

References

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Hans

Hans,

I think you must have intimidated everyone by the amount of information above...lol!
Here's my small contribution.... I understand that hawthorn works as an ACE inhibitor.

Joyce

Hans,

Thank you for presenting this topic. Also, thank you for your detailed article verifying the fibrosis / a-fib association, also the aldosterone / inflammation / fibrosis connections.

Another article, presented to this forum by Jackie in February:

Cardioreparation in Hypertensive Heart Disease by Karl T. Weber, MD., Division of Cardiovascular Diseases, Department of Medicine, University of Tennessee Health Science Center, Memphis.
http://hyper.ahajournals.org/cgi/content/full/38/3/588

"Cardioreparation" -- now there's a hopeful word. The topic is controlling hypertension by reducing/eliminating cardiac fibrosis via ACE inhibitor drugs. "Cardioreparation" has me up to my optimistic eyeballs looking for confirmation of my sense that something like that has been taking place in me "naturally", not with drugs, ever since I was blessed to "kick the beast" >2 1/2 years ago.

Just the other day, Jackie did an outstanding service by providing, on the Bulletin Board, extensive documentation showing that Mg deficiency (MgD), definitely a lead-up to my 10 years of dysrhythmias, encourages/causes fibrotic changes in cardiac tissues. Mg level restoration was definitely a big part of overcoming my a-fib. Since then the stability of my heart seems to have been steadily increasing, so that today there are virtually no strange "ectopic" beats remaining -- they had remained in full force after AF left. To explain this, I would sure like to understand a mechanism for spontaneous internal "cardioreparation", and to have others benefit from it. Did MgD make my atria fibrotic? Was atrial fibrosis the root cause of my a-fib? Did making Mg normal have a hand in reversing fibrosis, and is it continuing to do so?

Dr. Andrew Weil's 'Spontaneous Healing' (1995) gave me initial encouragement to look for ways to encourage my body to heal itself from a-fib, and it happened. Since then I have been enthusiastic about trying to understand the mechanism. This forum has provided a great opportunity for assistance in understanding from others, so I'm really optimistic about further important reflections and conclusions from the thoughtful participants. It would certainly be rewarding if judicious use of ACE inhibitor drugs would be shown to be useful in reversing a-fib, also if Mg might do the same; it seems that so far the only hope is in controlling it. Even PVI ablation does not alter the substrate that somehow, for most, was made able to fibrillate following many normal rhythm years -- 64 for me. If deleterious remodeling continues, who can say about the future?

Erling

Jackie,

I decided to switch over from the BB to the CR.

From your BB post to me: "What we are now looking to find is specific information about which enzyme is affected with magnesium deficiency that results in reduced proteolytic or fibrinolytic enzymes and allows fibrosis to fluorish. This will be a major find if it surfaces."

Would someone be able to run this by Mildred Seelig. M. D.?

Also, my question about the generalized distribution or specificity of fibrosis in the body was prompted by the association of fibromyalgia with trauma (in some cases, psychological) and surgery. As I understand it Fibromyalgia

occurs non-specifically, that is, throughout the body.

Carol

Carol - sorry, I didn't get back to this post..... eventually, we may run it by Mildred Seelig, but first a bit more investigation.

Second...if you can get into Dr. Wong's web page and locate his article on fibromyalgia, I think you may learn your answer. He's an expert on FM since he suffers from it.

http://www.life-enthusiast.com/enzyme/wong_biography.htm

Jackie

Carol - Sorry - try this web page

http://www.totalityofbeing.com/ArchivedFibroRealArt.html

At least if you went to the other, you could read his Bio.

Jackie

Aloha

I find the present CR topic most titillating. However, the emphasis on the aldosterone/cardiac fibrosis connection with respect to LAF in my humble opinion misses the mark.

I have always maintained that cardiac fibrosis is way too nonspecific to manifest as atrial fibrillation at least in the absence of other measurable cardiac disease, i.e., LAF.

On 8/21 Erling posted an interesting article entitled

Enalapril Prevents Perpetuation Of Atrial Fibrillation By Suppressing Atrial Fibrosis And Over-Expression Of Connexin43 In A Canine Model Of Atrial Pacing-Induced Left Ventricular Dysfunction.
Sakabe M, Fujiki A, Nishida K, Sugao M, Nagasawa H, Tsuneda T, Mizumaki K, Inoue H.
Second Department of Internal Medicine, Toyama Medical and Pharmaceutical University, Toyama, Japan.
at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15167279&dopt=Abstract

Enalapril is an ACE (angiotensin converting enzyme) inhibitor. So, anything that stimulates the RAAS (renin angiotensin aldosterone system) could potentially be aggravating AF via overexpression of connexin 43. Perhaps in the etiology of LAF aldosterone (the second A in RAAS) and its effect on blood potassium (and cardiac fibrosis) is secondary to angiotensin (the first A in RAAS) and its effect on connexin.

A word on connexin. At some point in the past I think Erling has mentioned gap junctions. For a good review please visit http://circres.ahajournals.org/cgi/content/full/91/2/85 Connexin Diversity, Discriminating the Message
Mario Delmar, Department of Pharmacology, SUNY Upstate Medical University, Syracuse, NY.
Circulation Research. 2002;91:85.

Gap junctions function at least in part as ion channels. Suffice it to say that connexin 40 and 43 are the two gap junctions found in the atrium and connexin 43 confers 10 times greater potassium permeability than connexin 40.

“One theory suggests that conduction is analogous to that through continuous linear cables.9 The conduction system is made up of myocyte cells and gap junctions. Gap junctions are proteins that form discrete ion channels between

myocytes. The density of gap junctions is higher in the direction of fiber orientation (longitudinal) than at right angles (transverse). A decrease in gap junction density may be an important basis for dysrhythmia in cardiac muscle.9"
9. Grant AO. Basic cardiac electrophysiology. In Naccarelli GV, ed. Electrophysiology Self-Assessment Program. Bethesda, MD: The American College of Cardiology; 1996:1.31.25.
http://www.aacn.org/AACN/jrnlci.nsf/0/10fe3dec676e01cc88256652006017af?OpenDocument

Other research has shown that the density of gap junctions in those with AF compared to those without are more dense in the transverse direction.

This would seem predictable since not only waves propagated by PACs but also wavelets created during AF produce more "transverse" activity v. the usual longitudinal direction of waves propagated during NSR. This arrhythmic activity might drive gap junction remodeling.

We all know about the role of potassium in LAF and the connexin/potassium connection would seem to further implicates gap junctions in LAF. I find this more specific connection between angiotensin/connexin and LAF more palatable than the RAAS/fibrosis approach. However, although I don't profess to know exactly how it works, perhaps connexin 43 overexpression creates greater difficulty to maintaining intracellular cardiac potassium.

Perhaps connexin polymorphisms and their regulation of atrial muscle cell potassium permeability are at the heart of LAF. This could be the more widespread genetic predisposition about which we've talked. Connexin overexpression via RAAS could be the potentiator in those predisposed.

Other pertinent articles include:

Association of Human Connexin40 Gene Polymorphisms With Atrial Vulnerability as a Risk Factor for Idiopathic Atrial Fibrillation.
Firouzi M, Ramanna H, Kok B, Jongsma HJ, Koeleman BP, Doevendans PA, Groenewegen WA, Hauer RN.
Department of Medical Physiology, University Medical Center Utrecht; Department of Cardiology, University Medical Center Utrecht; Complex Genetics Group, Department of Medical Genetics, University Medical Center Utrecht; and the Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands.
at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15297374&dopt=Abstract

Gap Junctional Remodeling In Relation To Stabilization Of Atrial Fibrillation In The Goat.
van der Velden HM, Ausma J, Rook MB, Hellemons AJ, van Veen TA, Allessie MA, Jongsma HJ.
Department of Medical Physiology and Sports Medicine, University Medical Center Utrecht, The Netherlands.
at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=10912458&dopt=Abstract

Mahalo

PC v55

Hilsen, PC

Very interesting about gap junctions as ion channels, and increased transverse density in AF. Thanks for that.

You maintain that "cardiac fibrosis is way too nonspecific to manifest as atrial fibrillation", but Dr. Van Wagoner says "It is evident that fibrosis can isolate muscle bundles, and that this can alter the pathway of electrical activation, creating a substrate that can promote the persistence of atrial fibrillation." (Innovations: Research in Atrial Fibrillation http://www.clevelandclinic.org/heartcenter/pub/atrial_fibrillation/AFresearch.htm)

How to reconcile -- am I missing something?

Erling

Hi Erling,

I certainly don't disagree with Dr. Van Wagoner on that point. There are many articles that testify to the dispersion of refractoriness amongst other things caused by cardiac fibrosis. However, I think he's talking mainly about AF not LAF.

My problem for LAF is why don't we see at least some sign of mild end organ ischemia due to the decrease in cardiac output caused by the fibrosis or perhaps early signs of increased RAAS activity again due to this decrease in cardiac output. Unless, of course, you point to LAF as an early warning indicator of excess RAAS activity. But what about mild hypertension, etc., which would make it AF and not LAF.

And exactly why does a drop in blood potassium potentiate episodes if mild cardiac fibrosis were the only abnormality. I'm sure that subclinical cardiac fibrosis has to be much more common than LAF.

Subclinical cardiac fibrosis may be associated with AF in some but IMHO it doesn't adequately explain the burgeoning epidemic of LAF.

PC

PC,

Thanks. This is interesting. (Fish gotta swim, birds gotta fly -- man's gotta ask, why? why? why?)

Wouldn't a drop in blood potassium, with the attendant shortened ARP, be even more apt to potentate AF if the myocardium is fibrotic? Won't they be additive?

Dr. Van Wagoner again:

Basic Mechanisms of Atrial Fibrillation
http://www.ccjm.org/pdffiles/VanWagoner.pdf

"... fibrosis is associated with broadening of the P wave on the ECG and impaired ("zig-zag") conduction within the atria. Thus, in the presence of an initiating ectopic beat, it is easy to understand how more fibrotic atria would be more likely to sustain AF ... the extent of fibrosis in the right atrial appendage correlates positively with patients age and with the occurrence of AF after surgery ... fibrosis primarily increases the heterogeneity of conduction, with little change in the cellular electrophysiologic properties of the atrial myocytes."

Also, "Pretreatment of experimental animals with an ACE inhibitor attenuated, but did not prevent, the increase in atrial fibrosis. It is therefore uncertain whether atrial fibrosis, once developed, can be reversed. This poses a major challenge to the pharmaceutical management of AF in older patients."

Erling

Erling,

Again I agree with everything you've said.

This is only my opinion on a disease that is a real conundrum.

My basic approach to understanding a problem is to search for an explanation that fits all the observations. Why invoke two mechanisms where one might suffice?

I think subclinical cardiac fibrosis (subclinical because otherwise we're dealing with AF not LAF) is kind of like wrinkles. Everybody has some. But not everyone has LAF. So it would seem that something else is going on. Given the normal range of blood K from 3.5 to 5.0 mmoles/liter suggests that normals blood K varies quite a bit, yet "normal" people do

not have LAF.

Your referenced quote above states:

"...fibrosis primarily increases the heterogeneity of conduction, with little change in the cellular electrophysiologic properties of the atrial myocytes."

So, if fibrosis is integral in the genesis of AF, there has to be something else going on as well in us LAFers.

PC

PC and Erling - Thanks for the lively dialog....

Excuse my mundane attempt at defending the reason for my excitement over making a case for the magnesium deficiency/fibrosis connection…..

PC… are you saying that magnesium deficiency in an LAFer does not contribute to fibrosis without some other underlying factor…which would then reclassify to AF not LAF?

It's probably not as simplistic as this, but when I read this article (hypothesis) (below)…. it seemed reasonable to me to suspect magnesium deficiency could lead to some amount of fibrosis which would sustain ongoing AF …In Erling's case, once the Mg deficiency was corrected over a period of several years, he was able to regain and sustain normal sinus rhythm.

My excitement was over a possible connection that with additional magnesium enabling sufficient production of fibrinolytic enzymes once again, the (probably) small amount of existing fibrosis was eliminated by the natural lysing action that takes place in younger bodies with adequate enzyme production. Dr. Wong (of my CR post) indicates enzyme production wanes around age 27…

Model of cardiovascular injury in magnesium deficiency.
Med Hypotheses. 2001 Jan;56(1):110-3.

Magnesium deficiency is known to produce cardiovascular lesions. It is, however, not clear as to what constitutes magnesium deficiency - reduced serum levels, reduced tissue levels or reduced intracellular levels of the ionic form of the element.

This article cites evidence in support of a hypothesis that a fall in serum magnesium levels may trigger a temporal sequence of events involving vasoconstriction, hemodynamic alterations and vascular endothelial injury to produce pro-inflammatory, pro-oxidant and pro-fibrogenic effects, resulting in initial perivascular myocardial fibrosis which, in turn, would cause myocardial damage and replacement fibrosis.

Further, angiotensin II may be the prime mover of the pathogenetic cascade in magnesium deficiency. Importantly, such a mechanism of cardiovascular injury would be independent of a reduction in myocardial or vascular tissue levels of magnesium.

PC brings up a point I haven't spent much time considering….the distinguishing of AF vs. LAF…. I've probably been assuming that most posters here are LAFers…. and apparently this is not the case…or so says Dr. Van Wagoner in the Basic Mechanisms of AF article Erling references….

Van Wagoner says " "In a MINORITY of patients, AF exists in the absence of structural heart disease or OTHER

APPARENT RISK FACTORS".....(my emphasis)

So I am wondering…is intractable magnesium deficiency enough of a factor to reclassify LAF to AF? Also along that line, then, would elevated levels of C-reactive protein (and inflammation)– seen prevalent in people with AF also be a factor to reclassify….or that of elevated Homocysteine?

If so... then... what you say PC...."So, if fibrosis is integral in the genesis of AF, there has to be something else going on as well in us LAFers." Might this not be Mg deficiency? Elevated CRP or Homocysteine that creates the inflammation and a fibrotic response?

I'm going to have to think a while on the gap junctions.

PC – how goes the hula lessons?

Best regards,
Jackie

Jackie,

Van Wagoner is correct. AF without underlying heart disease (lone atrial fibrillation) is found in a minority (about 20%) of the AF population. Underlying heart disease is the norm rather than the exception. However, among the afibbers involved in afibbers.org about 93% have no underlying heart disease. I should think that this is the population that should concern us in our research.

Hans

Hi Jackie,

I've been shirking my hula lessons, but the sailing, canoeing and kayaking are going swimmingly so to speak.

I certainly don't have a problem agreeing with everything you and Erling have posted thus far.

Mg deficiency in an LAFer may well cause fibrosis. It's just that in the absence of some marker specific for cardiac inflammation or a cardiac biopsy (rather drastic) showing fibrosis, whether or not there is demonstrated Mg deficiency, the AF must at present be classified as lone. CRP, homocysteine, etc., are certainly correlated with cardiovascular problems, but are not sufficiently specific to indicate definite cardiac disease, unlike an elevated blood pressure reading, heart failure or enlarged heart on a chest X-ray, etc.

In fact they are more correlated with vascular disease than actual cardiac disease. Of course, atherosclerosis of coronary arteries can lead to cardiac fibrosis, but then again it would no longer be lone AF.

Mg deficiency is definitely tied to the potassium problem (and perhaps cardiac fibrosis too) in LAF, but 80+% of the population is Mg deficient and yet LAF is nowhere near that prevalent.

So, it seems to me that in us LAFers there must be something else going on over and above cardiac fibrosis. I think that something else may possibly be overexpression of connexin 43 in the atrium caused by RAAS. A genetic polymorphism might possibly make some of us predisposed to this development. The gradual deterioration, i.e., increasing frequency and duration of episodes, would appear to be due to remodeling. Perhaps this might involve gap junctions. All that you both write on the fibrosis, magnesium deficiency is probably also at work.

Again, Jackie and Erling, this is just my understanding of the disease and thoughts on its possible genesis. All the points that you both continue to contribute are invaluable in maintaining optimal health. LAF is a very small sector (100% for some of us unfortunately) of this in general. Why is the number afflicted so small, given the prevalence of Mg deficiency and probably subclinical cardiac fibrosis as well.

PC

Hans and PC - Thanks for your input..... and I agree, Hans... LAF should be focus of our research, and I'm glad to have you confirm that 93% of our members are LAFers.

Obviously, there is some hidden or obscure connection that hasn't been studied and proven to be directly casual to LAF. Otherwise, we wouldn't still be turning over every stone looking for clues.

I like the genetic polymorphism predisposition hypothesis, PC, because current work in this area is indicating that some of these gene defects can be reversed or corrected.... so say the researchers at Metagenics who are working with genomics and nutritional intervention.

We can't argue about the numbers you compare....we are a small number... a chosen, select few with AF and, most likely, magnesium and potassium insufficiency.....and as you say some other contributing factor or factors besides or in addition to fibrosis.

PC - are you aware of many studies on your suggestion....."may possibly be overexpression of connexin 43 in the atrium caused by RAAS." Perhaps if these are available via Internet resources, we could delve into this area.

PC - it's wonderful that you are enjoying more than just the hula...which sounds pretty tame compared to life on the surf. I'm so happy for you.

Be well.

Thanks for your input.

Regards,
Jackie

Cardioreparation, zowie. I sure hope so. But about ACE inhibitors reversing afib, i don't think so, and my reason for saying that is that at the time of my first afib attack, i had been taking 10 mg of lisinopril more or less faithfully for several years. Of course, my diet was very poor during those years where magnesium and potassium were concerned, and i ate a lot of plastic food containing the usual chemical soup those things contain, and a really lot of high glycemic load foods too. So maybe it would have been worse if not for the lisinopril, i don't know.

"...mild hypertension, etc., which would make it AF, not LAF." Please will somebody clarify this for me? When i first got afib, my doctor knew i had high blood pressure, because she wrote me the prescription for lisinopril. I have told every doctor i have seen since, too. Is this a matter of their ignorance, that they thought i had LAF rather than AF? They all told me the bp had nothing to do with anything, and nothing was wrong with me. Then, of course, we would get into the usual fruitless discussion about if there is nothing wrong with me, why is my heart doing that? The uniformity of the i-don't-know responses was my first clue that i had better learn something about this myself.

Now that i am not having afib episodes any more, i suppose it doesn't matter whether what i had was AF or LAF, but it does make me curious which one.

PeggyM

Jackie,

Thanks much. Life is certainly more enjoyable here in the islands.

Regarding my statement about "... overexpression of connexin 43 in the atrium caused by RAAS", I was extrapolating

from the article that Erling had cited. It was entitled "Enalapril Prevents Perpetuation Of Atrial Fibrillation By Suppressing Atrial Fibrosis And Over-Expression Of Connexin43 In A Canine Model". This suggests that the RAAS might be the culprit in LAF. Unfortunately I don't know of any other references on this possible RAAS/connexin 43 link.

Although the genetic predisposition certainly could be a polymorphism, it may not even be necessary to invoke that. Connexin 40 and connexin 43 represent the vast majority of gap junctions in the heart. Each gap junction has five connexins. Perhaps LAFers have more C43s and those not so afflicted have more C40s. If indeed C43 is 10x more permeable to potassium than C40, as research indicates, then the intracellular/extracellular potassium gradient becomes especially critical. When blood K levels are low, intracellular K would be constantly leaking out via these gap junctions composed predominantly of C43.

Most gap junction occur in the direction of of waves propagated from the SA node (NSR), i.e., longitudinal. The increased density of transverse gap junctions in LAFers (v. normals) would seem to add epidemiologic evidence to the above physiologic connection.

It would appear that connexin 43 expression can be downregulated by suppressing the RAAS. This might just be enough to suppress AF episodes. We can't change the C43s to C40s, so our predisposition would continue to lurk in the background, awaiting our dietary and hydration indiscretions.

PC

"...but are not sufficiently specific to indicate definite cardiac disease, unlike an elevated blood pressure reading, heart failure..."

So an elevated BP reading is considered a cardiac disease. I never realized that before. Thank you, all.

PeggyM

Hans,

Is mild hypertension considered a heart condition? I am still trying to classify myself here.

PeggyM

Peggy,

Essential hypertension (the common kind not involving a narrowing of the aorta) is generally considered to be a disorder of the cardiovascular system. Since it primarily involves a kidney dysfunction, not a heart problem, I don't see how it could be classified as a heart condition.

I hope PC will correct me on this if I am wrong.

Hans

I guess i'm confused between mild hypertension [which i understand to be pressures not more than 140/80] and essential hypertension. Is what i have got called mild essential hypertension? Essential hypertension being hypertension not caused by some other illness, when it would be called secondary hypertension. Is that right?

I think that means that if i had the kind of mild hypertension spoken of above, which is a cardiac disease, then i would have AF, not LAF. But i have mild essential hypertension, so therefore what i had when i was still having afib, was LAF, not AF. I think.

You know, i can tell there is a problem with the above, but it's as clear as mud to me, and i wish one of you excellent people would straighten it out.

PeggyM

Peggy,

Essential hypertension is not a cardiac (heart) disease, but a cardiovascular disorder with emphasis on the vascular. It involves endothelial dysfunction - an abnormality of arterial walls, but is primarily a kidney problem. Yes, you could classify your condition as mild essential hypertension, but that still does not make it a heart disease and if you have no underlying heart conditions then your atrial fibrillation is LAF, not AF.

Hans

Peggy

Lone atrial fibrillation is traditionally defined as AF without organic or structural heart disease. The workup to exclude organic heart disease usually includes history, physical examination, CXR and ECG, as well as transthoracic and transesophageal echocardiography.

The problem with a dogmatic black and white answer to your question is that it ignores the continuum or gray zone between good health and disease. Hypertension is an important predictive factor for AF. It can damage the aorta and the rest of the vascular tree, including the coronary arteries. It can also lead to an enlarged atrium. Indeed, if one goes further and actually evaluates intracardiac hemodynamics in those with LAF by the above definition, diastolic left heart dysfunction is often detected.

Most cardiologists would not consider AF with hypertension to be lone, especially in an older patient. Besides the real bugaboo with LAF is its stroke risk. Hypertension without AF is a definite stroke list. So don’t lose sight of the forest for the trees. Don’t worry about whether you are technically considered LAF or AF, especially if you only have mild hypertension. Just keep that BP under control.

PC

Peggy,

I absolutely agree with PC. Whether or not one can be classified as having LONE atrial fibrillation or atrial fibrillation is not a black and white situation. The average age of diagnosis for lone afibbers in our group is about 46 years. At that time it is probably correct to designate the AF as lone provided no organic or structural heart disease has been detected. And yet, even that is a bit murky as it depends very much on how thoroughly the individual was tested.

As we age it becomes more and more likely that some of the deteriorations that PC mentions can be found in most hearts – by age 65 most of us are probably not entirely LONE anymore even though we may not have been officially diagnosed with a heart condition. So it is quite likely that elderly afibbers will approach the category of plain old atrial fibrillation, ie. atrial fibrillation accompanied by some underlying heart problems. The likelihood of such problems being present would increase if hypertension is present.

Nevertheless, I think we should, for classification purposes, continue to use the term lone atrial fibrillation for afibbers who have not been officially diagnosed with heart disease or structural abnormalities. I don’t think it is reasonable that we should arbitrarily have to “retire” from the LAF group just because we reach the age of 65 years. However, in our research we should be mindful that it is likely that some aspects of atrial fibrillation, such as fibrosis, become more likely as we age.

I hope this clarifies the situation and thank PC for his sage input.

Hans

Hi Erling,

I am following this Conference topic with great interest. Sorry about the "shot across the bow" with your's and Jackie's reply to my Mg toxicity post the other day. I wanted to start a bit of a lively discussion about Mg as there are many conflicting views and about its use and side effects. I think I succeeded.....

Jackie replied that my kidneys might be in poor shape but several weeks ago I had blood, urine and an ultrasound scan of upper abdomen and kidney function was normal. The only thing revealed was that I have a fatty liver. (my GP said he had 2 other patients with LAF and they also were diagnosed with fatty liver.....). I have been thinking about why the Mg sent my blood pressure up and increased pac's and palpitations. I was taking Losec, an Mg based drug, for my GERD 2 years prior to starting Mg supplementation. I think the Mg in the Losec combined with my dietary changes that consisted of cutting out nearly all dairy (Ca), and increasing the amount of vegetables and nuts sent me into hypermagnesemia.

Anyway, since stopping the Mg supplements I have been running around like a spring lamb. No pac’s , palpitations, tachycardia. Just a normal heart. No afib now for 17 months.

I know many afibbers on this board have been taking regular Mg supplements but at the same time have been altering their diets, cutting back dairy (Ca) and eating healthier. Maybe their Mg supplement dose should be changed (lowered) to reflect their dietary changes? I bet many haven’t done this.

As there is conflicting information about this whole Mg issue the best thing would be for all us afibbers to do an in depth survey on Mg use and its effect, for better or worse, on our bodies and hearts. It would give you guy’s doing research some positive information to go on.

Dean

Dean - Running around like a spring lamb is definitely a good report. Congratulations....on that as well as the healthy kidney check.

I'm really glad to have your participation - bringing up good observations - and good questions.... after all....that's the way we find solutions...explore all possibilities and re-examine continually.

I remain thoroughly convinced that the importance of adequate electrolytes such as magnesium and potassium are essential in one's evaluation at the onset of AF. Refinements and re-evaluations are also essential on a continual basis to be sure one doesn't go on overload - as was your case.

Here, we can only speak in generalities, but ultimately, the monitoring has to be done with lab work and it would be foolish to assume otherwise.

You mentioned the correlation with fatty liver and AF..... I'm musing that this has to do with faulty metabolism of glucose, leading to dysglycemia, insulin resistance, metabolic syndrome and down the road, frank Type II diabetes. Fatty liver is definitely part of this scenario.

And, the initial beginnings of dysglycemia manifest in hypoglycemia which can and does trigger AF. Some people don't get AF but many will proceed down the metabolic syndrome path.

I hope you take immediate steps to begin to correct the fatty infiltration situation you have with the liver. This is extremely important.

Be well...and please continue to think critically and offer your timely observations. One size does not fit all and the more we learn about the deviations, the better equipped we will be to handle all possible facets of curing AF without ablation. That's a noble goal.

Carry on.

Jackie

Dean,

Thanks for following along. My contribution to our little set-to the other day was by challenging some of your statements, one being your doctor "... gave me quite a lecture about Mg toxicity to the kidneys." I was hoping for a response -- perhaps later? This is a bit "off-topic", but since this forum's resident pathologist PC, MD is here with us, perhaps he will address this?

Erling

Dean,

I certainly agree with Erling on the Mg toxicity statement. Your doctor is the one that needs the lecture.

At a recent IRB (Institutional Review Board) meeting I attended (before I retired) a related topic was discussed and approved.

Most hospitals have this kind of committee to review and approve or not research programs that involve patients. Our mission is to act as a patient advocate preserving their privacy, rights, etc., while enabling ongoing efforts to improve our collective well being. The committee acts as a watchdog.

The program that we were discussing was called Fast Mag. Through it paramedics and emergency personnel were to administer IV Mg at the scene to any patient with a recent stroke. I specifically inquired about whether they were concerned about renal function in such situations. After all most stroke victims would be in no position to respond. I knew that renal function should not be a problem in the vast majority of cases, but I just wanted to hear what the MD panel presenting the project would say. It turns out that our area was rather late in implementing this policy, which is standard in many other parts of the country. In fact the policy includes IV infusions on an almost hourly basis during the acute period.

Of course, renal toxicity can rarely occur, but foregoing Mg in such situations is like throwing the baby out with the bathwater. So, I would not hesitate an instant to advise Mg supplementation up to bowel tolerance. But if this does not "agree" with you, always listen to your body, as you have.

Fear of potassium toxicity secondary to supplementation is much more entrenched amongst practicing MDs. Much of this is medicolegal. If this were to occur, there would be no defense.

But, as you may learn from Hans' upcoming AFIB Report, we may all be throwing out the baby with the bathwater on this issue as well.

For a good review on the latter please read "Importance of Potassium in Cardiovascular Disease" by Domenic A. Sica, MD; Allan D. Struthers, MD; William C. Cushman, MD; Mark Wood, MD; John S. Banas, Jr., MD; Murray Epstein, MD The article can be accessed at the below hyperlink, but you may be asked to register with medscape, a freebie.

http://www.medscape.com/viewarticle/438088?WebLogicSession=PgiB3VCzdZlfgYNlxX7UIXbKhPkKInWcfRfacD5B9B2LQxsWSsXZ|1343260868989756938/184161393/6/7001/7001/7002/7002/7001/-1

PC

PC,

Re: Fast Mag, you say "Of course, renal toxicity can rarely occur". What is the definition of "renal toxicity" as used here? Is it structural/functional damage to the kidney? If so, might it be permanent? Could such "renal toxicity" be incurred via oral supplementation?

Thank you.

Erling

Erling,

What I meant by the poorly chosen term renal toxicity (after all, how can the kidney be toxic?) was magnesium toxicity secondary to poor renal clearance of magnesium. As far as I know, magnesium toxicity has no renospecificity.

PC

PC,

Meaning, even with long term clearance of excess Mg, where the body cells just can't hold any more but one still keeps piling it on, there won't be any damage? Such as (pardon me) fibrosis?

Erling

Erling,

I think most of the manifestations of Mg toxicity are caused by the attendant electrolyte imbalance, i.e., neurologic and muscular (cardiac, smooth and skeletal) problems. These neurologic and muscular manifestations should be readily reversible, if the toxicity is immediately addressed. I'm less familiar with fibrosis. Perhaps Jackie can give a better answer on that. I was always taught that fibrosis is irreversible, but I don't really know the answer to that.

PC

I do want to talk about Dr. Wong's success in reversing fibrosis with proteolytic enzymes....but in the meantime... note this news article about a doctor in Australia reversing cardiac fibrosis.... and PC's pet -spironolactone…
.
Excerpts -

A common condition in heart failure can not only be arrested but reversed by a procedure that regulates salt and water in the body, Melbourne scientists have discovered.

Doctors say that the findings, on the condition known as cardiac fibrosis, could lead to a significant improvement in the treatment of heart failure, which causes more than 2700 deaths a year in Australia.

Morag Young, a senior researcher at Prince Henry's Institute of Medical Research, has found that blocking the hormone aldosterone not only arrests damage to the heart from cardiac fibrosis, but reverses it.

Medication that did this was available but not widely used because of side-effects, Dr Young said, with pharmaceutical companies now looking to redevelop the drugs.

She will present her findings today at the World Congress International Society for Heart Research in Brisbane.

One of its causes is cardiac fibrosis, a stiffening of the heart.

It is estimated that about 300,000 Australians have chronic heart failure, with 30,000 new cases diagnosed each year.

Aldosterone, which works in the kidneys to regulate salt and water in the body, is also important in blood pressure.

But Dr Young said her work showed that reversing fibrosis was independent of blood pressure - aldosterone could still damage the heart even if blood pressure was lowered.

She based her work on a large international trial of the aldosterone blockers, or spironolactone, in cardiac fibrosis patients. Known as the RALES trial, it found the drugs improved heart function and prolonged patients' lives.

Dr Young's study set out to discover why.
"What our study has shown is that maybe we should be recommending these drugs, because maybe they are having quite an important effect," she said.

Murray Esler, an associate director of the Baker Heart Research Institute, said the findings could be significant. "It would certainly improve the treatment of heart failure and, if the drugs were used widely, it could have a preventative effect also," Professor Esler said.

http://www.theage.com.au/articles/2004/08/08/1091903444873.html?oneclick=true

Jackie

“A magnesium deficiency causes an increase in aldosterone production and subsequent hypokalemia (potassium deficiency). An excess of calcium ions (Ca++) can also increase aldosterone production because excess Ca++ increases the secretion of ACTH.”

In the discussion so far no mention has been made of excessive calcium intake. If hypomagnesemia is being discussed should not excess Ca, it’s antagonist, also feature in this discussion?
I say this because of a post I put on the bulletin board on 01-15-04 under Dean titled “Large quantity of Ca in early childhood”. Everybody replied that they had indeed consumed large quantities of milk and dairy products for quite a number of years. I have always had the suspicion that the massive quantities of Ca we consumed via Daisy the cow back in the 1950’s,60’s 70’s and 80’s is part of this LAF puzzle. The vast majority of the participants on this website come from USA, Canada, UK, Australia, NZ, Europe. All major dairy consuming countries.

If hypomagnesemia is implicated in fibrosis then surely excess Ca must be equally as responsible?

Many of us have had great success with LAF by cutting out or drastically reducing dairy products

So where is the balance between Ca and Mg?

Dean

Dean,

I too pondered up[on the ill effects of many years of excessive milk consumption and 20-40 Ca-laden indigestion remedy tablets per day. However, when I dug my intracellular results out.... not only was my Mg bottom of range (Red Blood Cell), but so was my Ca (Leucocyte)..... Tough to figure that one out!

PC

As regards your intriguing hypothesis regarding the RAAS and the C43s..... is there some prescribeable medication which suppresses the RAAS system which some of us AFrs should be looking at/trialling upon an experimental basis??

Mike F.

Hi Mike,

Yes, there are a bunch - enalapril, lisinopril, losartin, etc. These are all ACE (angiotensin converting enzyme) inhibitors. They suppress the part between the R and the A in RAAS. Suppressing the last A aldosterone is also good but it would not suppress the overexpression of C43.

Of course, you've heard me and many others preach the benefits of proper hydration and that would represent the most natural way to keep the entire RAAS relatively quiescent.

Hans may have more to say on this point. Rest assured that he will be much more complete in whatever response he makes.

PC

"We can't change the C43s to C40s, so our predisposition would continue to lurk in the background, awaiting our dietary and hydration indiscretions." You know i think those are very true words, a good explanation of how things are with people who have discouraged the afib boogies from roosting in our personal lives. I'm very pleased to have found this all out here. My thanks to all.

PeggyM

Wow, lots of replies here! I'll have to have a read and catch up with the debate.

In the meantime, and hopefully not duplicitous, I'm wondering about ectopy, AF, and fibrosis.

I get a lot of ectopy (20-200 per day as well as most days having a few short runs (few secs) per day of the same). Sometimes I go for hrs with none, and then I can one every few beats for half a minute or so. In fact, I've had ectopy for most if not all of my adult life, but have 'only' had 5 episodes to date (one per-year-ish for the last 5 years.

I'm wondering whether some folks here get hardly any ectopy/the same amount of ectopy as any member of the healthy population, BUT when they do get ectopy they almost always get AF. Conversely, are there a lot of folks like me who get quite a lot of ectopy with only the occasional AF being provoked by it?? Maybe it's down to fibrosis with the latter group having relatively little fibrosis and the former group having significant fibrosis???

Mike F.

Hi Mike,

The reason I've been looking at a fibrosis / AF connection is because it's something that can rationally explain my personal experience. You probably know my story: no dysrhythmias for 64 years, then beginning ectopics, then lots of ectopics and first AF at 67, last AF at 74 but still lots of ectopics, and back to no ectopics at 76. How to understand this up-and-back-down reversal, for which I am so very grateful?

I have great difficulty explaining it to myself by Mg or C0-Q10 or other nutrient increases / decreases / adjustments per

se, so I've been looking for deeper effects of the many years of poor nutrition, and the recent years of good nutrition + supplements.

My hypothesis, supported by the research that Jackie has located and pulled together, much of it presented in great detail to CR Session # 24 titled Cardiac Fibrotic Remodeling, also more recently additional supporting research that she posted to the bulletin board:

-- long standing Mg deficiency coupled with Co-Q10 deficiency from aging (highly simplified) conspired to reduce energy dependent synthesis of the endogenous Mg dependent proteolytic enzymes that ideally keep fibrosis in check.

-- fibrotic remodeling of the myocardium ensued, causing gradual derangement of electrical conduction pathways, the consequence ultimately being some ectopics, then increasing ectopics, then occasional outright a-fib and a-flutter, followed by more and more frequent attacks as the extent of fibrotic remodeling, now aided by AF itself, steadily increased.

-- having corrected the Mg and Co-Q10 deficiencies, along with other critical nutrient deficiencies, internal enzyme production increased, gradually degrading fibrotic infiltrations in the atrial muscle bundles causing the process to reverse.

What do you make of this, Mike?

Erling

Erling,

An interesting surmisal indeed.

"fibrotic remodeling of the myocardium ensued, causing gradual derangement of electrical conduction pathways, the consequence ultimately being some ectopics, then increasing ectopics"

It's the ectopy which interests me most at present. Can fibrotic remodelling of the myocardium cause ectopy? I would have thought that it was degradation of the cellular electrolytic balance and cellular membrane which would cause ectopy per se, with any subsequent fibrotic remodelling eventually allowing the ectopy to precipitate AF.

Whilst I am both intrigued and pleased that your regimen has eliminated firstly AF and then ectopy, I wonder just how much such a no-doubt well-researched and rigorous approach would help many other AFrs here..... It could well be back to the old 'we are all experiments of one' scenario..... although one would think there must surely be some degree of commonality between many of us here.

Good to have you back on board but without AF Erling,

Mike F.

"Whilst I am both intrigued and pleased that your regimen has eliminated firstly AF and then ectopy, I wonder just how much such a no-doubt well-researched and rigorous approach would help many other AFrs here..... It could well be back to the old 'we are all experiments of one' scenario..... although one would think there must surely be some degree of commonality between many of us here."

Mike, i think a bunch of these experiments of one are now producing results. Erling was the first, but a number of other people, using for the most part less well researched and less rigorous approaches, have gotten afib out of our everyday lives. It doubtless does lurk in the background waiting for us to get stupid again, but for now we are not having afib attacks. Personally i find this a tremendous improvement over the previous condition. I think there must be a subset of afibbers who only need to get electrolyte levels up, keep hydrated well, stop eating wheat and/or dairy, cut out plastic 'food', and reduce the glycemic load in their diets, in order to be free from afib. Some people do not seem to

need to include all these items in their regimes, but most do. I sure am glad i found this site and learned to do these simple things to stay healthy.

PeggyM

I have just completed a research report on the importance of potassium. The report will be published in the upcoming issue of The AFIB Report, but as it is relevant to the current discussion I decided to post it as well.

My thanks to PC for his advice and comments and to Peggy for her insistence that we all try low-sodium V8 juice.

Hans

THE IMPORTANCE OF POTASSIUM

Important: Please read this entire report before acting on its findings

Potassium is fairly abundant in the body with a total content of about 135 grams (3500 mmol). Most, 98% to be exact, is found inside the cells, while the remaining 2% or about 2700 mg is found outside the cells, more specifically in blood serum. Blood serum level is normally maintained between 3.5 and 5.3 mmol/L. Humans evolved on a diet rich in potassium and low in sodium, so the body is designed to retain sodium and excrete potassium. Homeostasis (level between 3.5 - 5.3 mmol/L or 3.5 - 5.3 mEq/L) is maintained by excretion through the kidneys matching oral intake and by shifting potassium between intracellular and extracellular compartments.

Unfortunately, our modern diet tends to produce sodium overload and potassium depletion (hypokalemia). Hypokalemia (potassium level below 3.6 mmol/L[1]) is a serious condition that has been implicated in many aspects of cardiovascular disease including atrial fibrillation, stroke, heart attack, hypertension, and sudden cardiac death (SCD). Hypokalemia is also a strong predictor of early death in heart failure. One study found that as many as 20% of all hospitalized patients have potassium levels below 3.6 mmol/L[1].

Drs. John Macdonald and Allan Struthers of Ninewells Hospital in Dundee, UK have produced an excellent summary of the many consequences of hypokalemia in relation to cardiovascular disease[2]. Among the highlights of their findings:

· Hypokalemia is intimately associated with ventricular ectopy (PVCs) and an increased risk of ventricular fibrillation. Both can be prevented by increasing potassium levels.

· High blood levels of potassium inhibit platelet aggregation and thus help prevent ischemic stroke.

· Adequate potassium levels retard the progression of atherosclerosis.

· Heart attack patients with low serum potassium levels are significantly more likely to go into ventricular fibrillation (often fatal) than are patients with levels between 4.5 and 5.5 mmol/L.

· Potassium supplementation can significantly reduce blood pressure in patients with hypertension.

· A low magnesium level (hypomagnesemia) increases potassium excretion and it is difficult to remedy hypokalemia without first attaining normal magnesium levels. One study found that 42% of people with low magnesium levels also had low potassium levels[1].

The Scottish researchers also outline, in considerable detail, what can be done to remedy hypokalemia. They suggest that supplementation with potassium, on its own, is unlikely to increase levels significantly. The problem is that increased potassium intake activates the renin-angiotensin-aldosterone system (RAAS) which promptly proceeds to generate large amounts of aldosterone which, in turn, causes potassium to be excreted and more sodium to be retained. They estimate that a serum potassium increase of just 0.25 mmol/L results in an aldosterone increase of 50-

100%.

Heart failure and heart attack patients should aim for a serum potassium concentration between 4.5 and 5.5 mmol/L. People without cardiovascular disease will probably be OK at levels between 3.5 and 5.0 mmol/L, but there is some evidence that levels of 4.4 mmol/L or higher are required to prevent atrial fibrillation. Dr. Mina Chung of the Cleveland Clinic recommends a minimum level of 4.0 mmol/L for afibbers[3].

It is of interest that Austrian researchers recently discovered that cardiac surgery-induced atrial fibrillation is significantly more common among patients with serum potassium levels below 3.9 mmol/L than it is among patients with levels of 4.4 mmol/L or greater[4].

The National Council on Potassium in Clinical Practice supports the recommendation of a minimum blood serum level of 4.0 mmol/L (4.0 mEq/L), but further suggests that an optimal level for patients without renal dysfunction would be 4.5 - 5.0 mmol/L[1].

For those with low potassium levels the Scottish researchers recommend supplementation with potassium and magnesium combined with an aldosterone blockade to prevent increased potassium excretion. There are four main approaches to blocking aldosterone production or counteracting the effects of an excessive production.

ACE Inhibitors
Angiotensin-converting-enzyme inhibitors prevent the conversion of angiotensin I to angiotensin II and thereby interrupt the RAAS system's efforts to produce aldosterone. Some of the more common ACE inhibitors are enalapril (Vasotec), lisinopril (Zestril), ramipril (Altace), and captopril (Capoten). Unfortunately, there is evidence that the aldosterone-blocking effects of ACE inhibitors may only be transient and that the body eventually finds a way around the ACE inhibition and produces aldosterone just the same[2].

Angiotensin II Type 1 Receptor Blockers
These medications act by preventing angiotensin II from docking at its receptors and thereby inhibit the formation of aldosterone. There is evidence that lone afibbers have more angiotensin II receptors in the left atrium than do non-afibbers, so blocking these receptors could be important for reasons other than the prevention of excessive potassium excretion[5].

There is actually evidence that valsartan (Diovan) reduces aldosterone levels and also some limited evidence that candesartan (Atacand) and irbesartan (Avapro) can help prevent or shorten afib episodes[6,7,8]. Thus, all in all, angiotensin II receptor blockers combined with potassium and magnesium supplementation may be worth evaluating for afibbers with low potassium levels and no indication of hyperaldosteronism.

Potassium-Sparing Diuretics
These help prevent the excretion of potassium through their direct action on the kidneys. Combining them with potassium and magnesium supplements should result in increased potassium levels. The two main medications in this field are triamterene (Dyrenium) and amiloride (Midamor).

Aldosterone Receptor Blockers
These work by blocking aldosterone (mineralocorticoid) receptors and thereby prevent aldosterone from doing its dirty work of excreting potassium at an excessive rate. The main pharmaceutical aldosterone receptor blockers are spironolactone (Aldactone) and eplerenone (Inspra). There is evidence that potassium and magnesium supplementation combined with these blockers increases potassium levels and effectively replenishes tissue levels of both potassium and magnesium[2]. Spironolactone and eplerenone work equally well, but spironolactone is far less expensive. Eplerenone can be used if side effects (gynecomastia, impotence, irregular menses or bleeding, and gastrointestinal irritation) are experienced from using spironolactone.

The findings of the Scottish researchers, to a large extent, fly against conventional medical wisdom. The medical profession has always considered potassium levels above 5.1 mmol/L a far greater risk of ventricular arrhythmia than levels below 3.5 mmol/L. Yet, the Scottish report points out that the risk of ventricular fibrillation is 8 times higher in heart attack patients with potassium levels below 3.5 mmol/L than it is in patients with levels above 4.3 mmol/L. It is

also generally considered a definite “no-no” to combine aldosterone receptor blockers and potassium-sparing diuretics with potassium supplementation, yet the report emphasizes that potassium and magnesium supplementation without concomitant aldosterone blockage is ineffective.

The suggestion that both approaches may be needed was also pointed out in a recent paper which concluded that a daily potassium intake (via supplements) of 9 grams combined with a spironolactone intake of 250 mg/day was required to raise serum potassium level from about 4.0 to 5.2 mmol/L in a group of patients with inherited long QT syndrome type 2. The authors of this report concluded that a sustainable, mild increase in serum potassium can be safely maintained by oral potassium supplementation and spironolactone[9].

Other researchers have, however, found that potassium supplementation, on its own, can indeed be effective in reducing blood pressure and the risk of stroke. Daily supplementation with 60 mmol (2.5 grams) of elemental potassium has been found to decrease blood pressure significantly over a 12-week period[10,11]. So if potassium supplementation decreases blood pressure, then it is obviously getting into the system. It should be pointed out though that about a third of the supplemented potassium was excreted in the urine indicating that the RAAS was activated by the supplementation[11]. Sixty mmol of elemental potassium is equivalent to 4.5 grams of potassium chloride, 6 grams of potassium bicarbonate, 7.5 grams of potassium gluconate or 20 grams of potassium citrate.

The National Council on Potassium in Clinical Practice recommends the use of oral supplementation with potassium chloride (800-2300 mg/day of elemental potassium) to replenish potassium, but point out that potassium bicarbonate may be more appropriate if metabolic acidosis is present[1]. If increasing dietary intake or supplementation does not bring potassium to the desired level, then potassium-sparing therapy with ACE inhibitors, angiotensin II receptor blockers, potassium-sparing diuretics or aldosterone receptor blockers may be added to the potassium supplementation regimen[1].

I am currently experimenting with spironolactone and potassium supplementation and have found that a potassium-rich diet (lots of fruits and vegetables) combined with 500 mg/day of elemental potassium (from potassium gluconate), 375 mg/day of elemental magnesium (from magnesium taurate), and 75 mg/day of spironolactone raised my potassium level from its usual 3.5-3.7 mmol/L to 4.5 mmol/L over a 1-month period. I should mention that I have been diagnosed with hyperaldosteronism, so plain ACE inhibitors or angiotensin II receptor blockers would probably not work for me. I am now attempting, with the cooperation of my physician, to optimize my intake of potassium and spironolactone so as to take the minimum amount of the drug.

I have also observed that I can completely eliminate ectopic beats and other uneasy feelings in the heart by drinking a special potassium drink. The drink consists of an 8 oz glass of warm water into which I dissolve a pouch of Emergen-C (containing 1000 mg of ascorbic acid + 200 mg of elemental potassium + 60 mg of elemental magnesium) as well as 1/4 teaspoon of potassium chloride providing about 1000 mg of elemental potassium. I drink this concoction over a 10-minute period and also use it to help swallow a 500 mg magnesium taurate capsule providing 125 mg of elemental magnesium.

Other afibbers have observed similar benefits by drinking low-sodium V8 juice. It would seem that the ingestion of a high potassium drink when increased ectopy is felt could help to avert a full-blown episode. The potassium drink could be particularly beneficial for afibbers whose episodes occur after a meal or when lying down to sleep. Research has shown that blood levels of potassium vary significantly during the day. It is as much as 0.6 mmol/L lower during the night than during daytime and also decreases substantially after ingesting a meal containing carbohydrates[1]. So having the potassium drink just before dinner or bedtime may be worth a try for these afibbers.

The high potassium drink may also be useful if consumed throughout the day for afibbers with the diarrhea type of irritable bowel syndrome. Diarrhea can lead to major losses of both potassium and magnesium as stool content of potassium can reach 90 mmol/L. Of course, consuming a potassium-rich drink throughout the day is likely to benefit all afibbers with serum potassium levels below the optimal range of 4.5 to 5.0 mmol/L.

CONCLUSION

Low serum levels of potassium (most likely accompanied by low intracellular levels) could be an important cause of

afib. Potassium supplementation may be required by some afibbers to bring their blood serum level up to the recommended range. It is possible that just supplementing with potassium and magnesium is enough to do the trick; however, if it is not, or if hyperaldosteronism has been diagnosed, then a combination of aldosterone inhibition and oral supplementation with potassium and magnesium would appear to be highly effective.

Moderate supplementation and increased dietary intake of potassium is likely to be safe for most people. HOWEVER, and this cannot be emphasized enough, aggressive supplementation and supplementation combined with aldosterone blockage SHOULD NOT BE UNDERTAKEN without the cooperation of a physician. Potassium levels need to be monitored regularly and potassium supplementation, if kidney dysfunction is present, can be fatal. Please take this as a SERIOUS WARNING!

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11. Gu, D, et al. Effect of potassium supplementation on blood pressure in Chinese: a randomized, placebo-controlled trial. Journal of Hypertension, Vol. 19, July 2001, pp. 1325-31

Some months ago Jackie posted that if you could “feel” your heart beat without taking your pulse, then you were probably short on K.

Recently Erling posted about a very rare, very brief episode of AF that was clearly triggered by a shortfall in potassium and hydration.

Also, recently Richard posted on “Are We Treating the Right Disease”.
http://www.medscape.com/viewarticle/463648_print
which posited that oxidant stress is responsible for AF through its effect on remodeling and the hypercoagulable state.

Perhaps instead of oxidant stress it’s an acute or chronic shortage of K.

Accordingly, I would like to add a few additional tidbits from the medical literature that further underscore these anecdotes and Hans’ timely and detailed posting on the importance of potassium.

1 Aldosterone change of 165% (v. supine) after 30 min of HUT (head up tilt).
Cardiovascular and Hormonal Changes with Different Angles of Head-up Tilt in Men
http://www.biomed.cas.cz/physiolres/2001/issue1/pdf/laszlo.pdf

I've always noticed that longer I stayed on my feet during the day, the more susceptible I became to an episode. Initially I thought that there was some vagal rebound after prolonged withdrawal of baroreceptor stimulation (standing). Now it would appear that there is is an additional mechanism. The drop in hydrostatic pressure sensed by the JGA (juxtaglomerular apparatus) in the kidney during prolonged standing (akin to HUT) may be causing significant loss of potassium via the attendant increased secretion of aldosterone.

2 Catecholamines and mineralicorticoids both cause urinary K (and Mg) wasting.

3 Insulin secretion can cause hypokalemia because insulin promotes potassium (and glucose) to enter skeletal muscle cells, liver cells, etc.

Initially I thought that postprandial episodes were due to primarily to the alkaline tide effect on blood K. While gastric cells are secreting HCl into the lumen to digest food, KHCO3 is being dumped into the blood to maintain intracellular electrical neutrality and pH. This would lead to increased urinary excretion of potassium. Hypokalemia both causes and is caused by alkalosis. Here again, we have an additional mechanism.

4 Hypokalemia causes an inability for the kidneys to concentrate urine.

This would lead to even more fluid loss, which would cause even more aldosterone secretion. Is it any wonder that endurance sports without proper hydration wreak such havoc on potassium physiology?

5 In cooking or canning foods, potassium is depleted but sodium is increased, as it is in most American processed foods as well.
Sodium chloride enhances insulin response to sugar ingestion.
Sodium induces catecholamine release.
Potassium also reduces cardiac sensitivity to catecholamines and angiotensin II.
Increasing potassium intake, even in the presence of high sodium intake, has an effect similar to that of reducing sodium intake. The benefits of reducing dietary sodium and increasing potassium may be additive, as the dietary ratio seems to be more important than the total dietary content of either.

6 Hypoglycemia causes an increase in ACTH secretion, which causes an increase in both cortisol and aldosterone
So, it would appear that insulin lowers blood K both directly (see #3) and indirectly (#6).

7 Hypokalemia causes both shortening of the refractory period and increased dispersion of this refractoriness.
These both loom large in creating an arrhythmogenic substrate.

I personally feel that hypokalemia exerts much of this effect through connexins (see earlier post). IMHO electrolyte imbalance (v. fibrosis) seems much more likely to trigger LAF, especially given its "nimble nature". Clearly anything that further disperses the heterogeneity of conduction, i.e., fibrosis, is additive.

Hans briefly mentioned "aldosterone escape", which is what happens when you use an ACE inhibitor or angiotensin blocker alone. Because aldosterone is controlled not only by the RAAS but also by the Na/K ratio (low ratio means more aldosterone secretion), the latter can assume a larger role in the regulation of blood K, when the former is blocked. For the same reason, K supplementation will not only increase aldosterone secretion due to a lower Na/K but also lower the component of aldosterone caused by RAAS activity. That's a good thing. And don't forget that ACTH is the third means by which the body regulates aldosterone.

Over the past month I've diligently searched the internet and contacted several international manufacturers of laboratory equipment to locate a portable potassium meter that can analyze as little as a drop of blood. As you know, highly accurate portable glucose meters are widely available. Two companies, Horiba and Hoskin Scientific, have such products. Unfortunately they are useful only in agronomy, due either to insufficient sensitivity (Horiba) or to specimen requirements (transparent for Hoskin). It's too bad that blood K measurement has not reached the popularity and demand that glucose enjoys. But keep your eyes open on this.

PC

Hans and PC - thanks so much for these valuable and very complete examinations about the role of potassium. I have an observation to share which fits right in.

Ever since the cardioversion after ablation, I have had more PVCs (I'm told) than I ever had previously.

After a particularly stressful day and without proper meals, I noted after the evening meal (which was proper and innocent of any possible triggers), that PVCs were active and then I had a run of about 20 quick beats. This settled into a pattern of a big thump every 30 beats. This was unusual and a bit unsettling and not wanting it to continue to become a new "milestone" for me.... I took 1/4 tsp. potassium chloride in warm water along with some magnesium.... probably about 600 mg.

Probably, I didn't need the magnesium, but I wasn't taking any chances.

Within less than 5 minutes after swallowing the potassium water, my irregular beat normalized and has been absent ever since!

So.... just one more testimonial that for whatever reason, potassium deficiency is definitely a contributor...and most likely THE most important consideration.

I now have a little sealed, waterproof vial of KCl powder that I'll carry around with me as my emergency stash in case this crops up again. It is possible that my ectopy might not have become anything more than just that, but I wasn't taking any chances.

PC - I think that you should be inventing this potassium meter now that you are retired.... I'll place my order now. Great idea.

Thanks again for this very substantial and supportive evidence in making the case for potassium deficiency.

Best,
Jackie

Jackie,

What happened to Emergen C. I bought some of that after you'd recommended it on the BB. I thought it was pretty good stuff.

Hans and I were just comparing notes on the same approach to ectopics that you follow.

Mahalo

PC

PC - EmergenC is still in my arsenal..... it's just that it only has 200 mg potassium....and I was wanting a larger "hit".... I just as easily could have added the extra KCl to the EmergenC..... I think it is a great product because of its portability and ease of adding to water anywhere at any time. I always carry some with me and have it for the golf course, as well.

Have you tried the new ElectroMix by the same company? It makes a liter of water into a Sports Water - instantly...and has a very slight lime taste...

Has less potassium though, in the form of potassium bicarbonate, only 100 mg. but it is nice to keep chilled and drink all day. Unlike EmergenC, it is not sweetened with fructose.

Jackie

This month in the *Italian Heart Journal* there appeared an article entitled “Pharmacological Treatment Of Atrial Fibrillation And The Underlying Substrate, The Role Of Angiotensin Converting Enzyme-Inhibitors And Angiotensin II Receptor Blockers In The Management Of Arrhythmias And Atrial Fibrillation”.
It is not very long and can be viewed in its entirety at http://www.italheartj.org/pdf_files/20040030.pdf

It seems to signal a new paradigm in the treatment of AF. LAF is not mentioned but LAF is not on the radar for most cardiologists. Many have never heard of it. This article is most pertinent to our plights nonetheless. The terms gap junction, ACEI (ACE inhibitors) and ARBs (Angiotensin Receptor blockers) figure prominently.

A few tantalizing passages from this article:

Besides the improvement of junction gap by enalapril, De Mello et al.5 reported that ACE inhibitors increase refractoriness of the heart reducing the incidence of ventricular and atrial arrhythmias.

Angiotensin II receptor blockers will reduce reentry arrhythmias by increasing junction gap conduction.

The incidence of arrhythmias is increased by angiotensin II by increasing electrical conduction resistance across the myocardium. This is due to the fact that angiotensin II increases junction gap resistance increasing reentry. Enalapril and losartan (angiotensin II receptor blocker) will decrease junction gap resistance producing a reduction of arrhythmias by reducing reentry.

Enalapril also reduces conduction velocity.

These observations point out that an intrinsic cellular renin-angiotensin system exists and has an influence in junction gap function. A reduction of gap junction conductance (as seen with angiotensin II) increases the incidence of reentry phenomena in the ventricles and atrium inducing ventricular and atrial arrhythmias like atrial fibrillation.

There is a new trend in using ACE-inhibitors and angiotensin II receptor blockers in the prevention of these arrhythmias.

PC

PC, Hans and you good folks with the higher brains I found this:
http://www.jafra.gr.jp/sumi5-e.html

In the present study, we first demonstrated that some components of natto had a lowering effect on blood pressure, by administrating natto extract to human subjects and rats. We administered a 80% ethanol extract of lyophilize viscous materials of natto. It was reported that the extract contains inhibitors of angiotensin converting enzyme (ACE), which converts angiotensin‡Tto its active form angiotensin ‡U(Fig. 1)1,2).

I have been using natto for over a month now and have dissolved a clot in a vein in my finger and the side effect was that I have lowered my BP quite a bit examples: 7/27 - 199/100; 8/14 - 185/96; 8/23 - 141/79;

Now my question can we use natto instead of ACE?

I tried Altace (Ramipril) for first 2 weeks in July and had to stop because of terrible side effects.

Thank you all for the wonderful information we are getting here,

Ella

Ella,

Most interesting observation. Nattokinase is indeed known to contain natural ACE inhibitors and to have a blood-pressure lowering effect. How much and at what times during the day do you take the nattokinase?

A couple of other thoughts:

1. Have you noticed any difference in your afib frequency and duration in the month that you have been taking the nattokinase?

2. What was your potassium reading prior to starting the nattokinase and is there any chance that you could have another potassium test now?

3. What brand of nattokinase do you take?

Hans

My afib still comes every 10-14 days
My last potassium test done march 23 - 04 was: 4.0 I will try and get another test done.
The brand I use is Natures Harmony Ingredients:
Nattokinase NSK-SD 800 FU* (equivalent of 40 mg) Cellulose.
*F.U is a measurement of activity of the Nattokinase enzyme.
I only took 2 a day, 1 in the afternoon and 1 before bed. It says for therapeutic effect 1 cap 3 times a day on empty stomach. More may be taken as needed up to 6 a day.

I will ask my Dr. if she thinks I should try 6 a day I will take some info on Natto to show her, hoping that she will do her own research.

Thanks
Ella

As I posted on the forum, I'm looking into getting hold of some Nattokinase to control my mild hypertension. I was given some Diovan (NOT valsartan as I said over on the forum), but have not taken it as it refers to part of its side effect profile as increasing K levels in the blood: I'm assuming that this will be detrimental in those prone to AF since the myocardial cells will (along with other cells) be leaking out their own K into the blood serum thus lowering intracellular K? As if those pesky C43s weren't enough of a problem!

I note that diovan is a angiotensin II antagonist. Forgive my ignorance here (due basically to not having enough time at the moment to do the necessary reading both here and elsewhere on the Internet), but does diovan fall into the category of drugs being discussed here?

Am I wise to avoid taking the diovan owing to its blood-serum-K-increasing side effect?

Regards (and much respect to you bright folks here),

Mike F.

Oops, sorry folks: I just re-read Hans' first post above. Stupid me. Diovan IS valsartan - which is, of course, one of the drugs being discussed here.

Whilst noting that valsartan might well be beneficial to those prone to AF, I am still concerned that it increases blood serum K. In so doing, I'm assuming that it must be depleting intracellular K..... is this a correct surmisal?? If so, that's

not some place an AFr wants to go. Am I missing something here? (Quite probably given my blunderings above (-:)

Mike F.

Mike,

Diovan does not increase potassium levels by causing intracellular leakage, but rather by preventing activation of angiotensin II and aldosterone and thereby preserving potassium. I think it is well worth a try; however, there is some indication that it might increase vagal tone. You should have your serum potassium level measured when you start it and for a while after and should also be very careful about deliberately supplementing with potassium, unless your level is below 4.4 mmol/L.

Hans

Hi Mike,

"Like ACE inhibitors, AT-II-receptor antagonists may induce hyperkalemia in patients with chronic renal failure and in those receiving potassium-sparing diuretics or potassium supplements. Although hyperkalemia and renal insufficiency are more likely to occur in certain at-risk patients (e.g., patients with severe congestive heart failure), serum potassium and renal function must be monitored in all patients. However, in clinical trials of AT-II-receptor antagonists, clinically important changes in serum potassium levels were reported for valsartan only."
from an article entitled The Renin angiotensin Receptor System at http://www.medscape.com/viewarticle/406895_12

Also, there is a nice rundown of costs of the various ARBs on p.14

There appears to be some controversy wrt the interaction between the vagus nerve and ACEIs/ARBs. More recent articles do not show any interaction at least in CHF patients. However, decreased vagal tone may occur via CNS AT1 receptor site binding of angiotensin. IF this were true than ACEIs/ARBs might increase vagal tone. Since most of the medical literature wrt vagal tone and ARBs/ACEIs has been collected from patients receiving these meds for their antihypertensive effects, their effects in LAFers remains to be seen.

A vagotonic property of ACEIs/ARBs would seem illogical, at least in LAFers. Angiotensin II is a potent vasoconstrictor, as well as stimulating aldosterone secretion, i.e., BP will increase. Consequently vagal tone will increase in response through the baroreflex. Therefore, it would seem to me that anything that blocks AT1s should be vagolytic not vagotonic. But what do I know?

I have sent an email to Professor De Mello, author of the article I posted earlier and at the absolute forefront of research on ACEIs/ARBs as antiarrhythmics.

PC

Hans and PC,

Thank you very much for your input. The thing which concerns me most is that valsartan might well INCREASE vagal tone - which is something I personally (as well as other VMAFrs) WELL do without. Not sure I like the fact that valsartan is the A11I which most interferes with serum K levels either. Seems like you can't get a med which has a distinct benefit without an attached downside also..... I'm inclined to work on my mild hypertension in other more natural and benign ways rather than popping valsartan..... at least pending the outcome of the discussion here.

Yours chomping on celery (and contemplating purchasing some nattokinase),

Mike F.

Hans, PC, Erling et al, this discussion would have attracted my attention anyway, but it is doubly interesting due to the connection between ACE inhibitors, potassium levels, and blood pressure. If i had known what i now do know about nutrition, i think i would never have gotten afib, because in remedying my high bp with increased potassium from diet [which would have increased magnesium and calcium too, they occurring in the same foods] i would very likely have not gotten to the point of depletion that gave me afib.

But what is also very interesting to me is that very few afibbers turn out to have high blood pressure. This is quite odd, because high blood pressure affects about a third of the population, according to recent news stories. I can only turn up 5 respondents here with hypertension, myself included. Can anyone explain why this is? If people can eliminate afib with better diet and electrolyte supplementation, as a number of us have now done, why didn't those formerly electrolyte-depleted people develop hypertension previous to afib, as i did?

How do afibbers differ from the general public, so that they typically have low blood pressure, rather than hypertension? Obviously afib is a symptom which can be caused by many different disease conditions, and i belong to a small subgroup, but what could cause this difference from the general population? If we could answer that question, we might have another puzzle piece.

PeggyM

Recently Jackie posted these PubMed abstracts on the bulletin board. Here are a few excerpts from the abstracts, also a 2001 Citation awarded to Dr. K. Shivakumar in recognition of his work on “Myocardial fibrosis in response to cerium and magnesium deficiency”.

Kumar BP, Shivakumar K, Kartha CC. Magnesium deficiency-related changes in lipid peroxidation and collagen metabolism in vivo in rat heart.
Int J Biochem Cell Biol. 1997 Jan; 29(1):129-34.

Magnesium deficiency is known to produce a cardiomyopathy, characterised by myocardial necrosis and fibrosis. ...Thus, the present study provides evidence of increased lipid peroxidation and net deposition of collagen in the myocardium in response to dietary deficiency of magnesium.

PMID: 9076947 [PubMed - indexed for MEDLINE]

Shivakumar K. Model of cardiovascular injury in magnesium deficiency.
Med Hypotheses. 2001 Jan; 56(1):110-3.

Magnesium deficiency is known to produce cardiovascular lesions. ...This article cites evidence in support of a hypothesis that a fall in serum magnesium levels may trigger a temporal sequence of events involving vasoconstriction, hemodynamic alterations and vascular endothelial injury to produce pro-inflammatory, pro-oxidant and pro-fibrogenic effects, resulting in initial perivascular myocardial fibrosis which, in turn, would cause myocardial damage and replacement fibrosis.

PMID: 11133266 [PubMed - indexed for MEDLINE]

C. Kumaran and K. Shivakumar* Superoxide-mediated activation of cardiac fibroblasts by serum factors in hypomagnesemia
Free Radical Biology and Medicine, Vol. 31(7) (2001) pp. 882-886

Magnesium deficiency is known to produce myocardial fibrosis in different animal models, but the underlying mechanisms are unclear. However, circulating levels of pro-oxidant and mitogenic factors are reported to be elevated

in a rodent model of acute magnesium deficiency, suggesting a role for humoral factors in the pathogenesis of the cardiovascular lesions. ... The findings are consistent with the postulation that serum factors may activate cardiac fibroblasts via a superoxide-mediated mechanism and contribute to the fibrogenic response in the heart in magnesium deficiency.

PMID: 11585706 [PubMed - indexed for MEDLINE]

Shivakumar K. Pro-fibrogenic effects of magnesium deficiency in the cardiovascular system.
Magnes Res. 2002 Dec; 15(3-4):307-15.

Magnesium deficiency is known to produce cardiovascular injury. A large body of experimental evidence supports the postulation that an immuno-inflammatory reaction and increased oxidative stress may damage the myocardium and vasculature in magnesium deficiency. Reparative/reactive fibrosis in response to the injury has, however, received little attention. Recent evidence from a rodent model of acute magnesium deficiency suggests that humoral factors may activate cardiac fibroblasts by a free radical-mediated mechanism and contribute to cardiac fibrogenesis. A similar mechanism may also promote cellular hyperplasia and increased matrix synthesis in the vasculature.

PMID: 12635886 [PubMed - indexed for MEDLINE]

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http://icmr.nic.in/award/icmraward_cit2001.htm

INDIAN COUNCIL OF MEDICAL RESEARCH

CHATURVEDI KALAWATI JAGMOHAN DAS MEMORIAL AWARD

2001 CITATION

DR. K. SHIVAKUMAR

The Chaturvedi Kalawati Jagmohan Das Memorial Award was instituted in 1975 by Dr. S.P. Chaturvedi in the memory of his parents. This prize is awarded once in three years to an eminent scientist, preferably a medical person, for his/her work in the field of Cardiovascular Diseases.

The Prize for 2001 is being presented to Dr. K. Shiva Kumar, Scientist-'E', Division of Cellular & Molecular Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, for his research work on "Myocardial fibrosis in response to cerium and magnesium deficiency".

The research work carried out by Dr. K. Shivakumar has led to the postulation of a neural pathway of activation of cardiac fibroblasts and delineation of a novel protective mechanism that may limit fibrogenesis in the aging myocardium and aetiopathogenesis of tropical endomyocardial fibrosis.

Dr. Shivakumar has more than 25 publications in reputed international and national scientific journals.

Erling

Jackie referred me to this CCF website for my GERD problems but on my reading so far there is much that may be applicable to this conference topic.

http://www.ccjm.org/PDFFILES/GERDDevault.pdf

Dean

More info on GERD and possible fibrosis link.

This is an extract from August afib newsletter about recent GERD research and its role in afib:

GERD involves a local inflammatory process that manifests itself as heartburn, regurgitation and difficult or painful swallowing. The researchers believe that it is the inflammation that affects LAF severity. They suggest several possible mechanisms:

-The local inflammation penetrates the esophageal wall and affects adjacent vagal nerves making them overly sensitive.

-The inflammatory process results in feedback to the brain leading to over-stimulation of the parasympathetic (vagal) branch of the autonomic nervous system. Vagal over-stimulation may lead to bradycardia and subsequent AF.

NOTE!!!!!**********The local inflammatory process penetrates the esophageal wall and spreads to the heart resulting in atrial myocarditis (inflammation of the wall of the atria). Biopsies in LAF patients have revealed that 66% of them suffer from myocarditis**********

-GERD may lead to the release of inflammatory mediators such as C-reactive protein (CRP). Many LAF patients reportedly have high CRP levels.

-GERD may induce an autoimmune response that contributes to LAF.

Thinking out loud here.....

- GERD is now increasingly common, due to our excessive Western diet, and most cases occur around middle age.
- Many if not most on this board have GERD or more importantly, undiagnosed GERD, and have linked this to afib attacks.
- From my previous post above, GERD is linked to pulmonary fibrosis and asthma and (from above) myocarditis.

If this is so then should not the aldosterone puzzle look more like this:

high aldosterone >>>>>>> GERD >>>>>>> fibrosis

This is a chicken and egg thing.....did the high aldosterone CAUSE the GERD first.....and THEN the heart fibrosis?

If so, would the answer be to lower the aldosterone level and treat the GERD with PPI drugs (as in my case and with great success) or surgery?

Research is linking GERD with more and more inflammatory health problems.

Dean

Dean - I only scanned this link...will go back and read... glad you found it useful...

In my fibrosis research.... it appears that the one link to fibrosis is inflammation... very clear. The body responds by laying down the fibrotic web. Several examples of firefighters being caught or trapped in intense heat/fire.... virtually immediate death by lung fibrosis.

On a small scale, then, we have increased or high levels of inflammation in our body...as measured by C-reactive protein serum analysis, we should make the link between that, elevated homocysteine and fibrosis... in this case, I'm thinking cardiac fibrosis.

Jackie

I'm sitting here in the office alone for the day getting board so I will annoy you people with more of my ravings. I just remembered, you are all asleep in the northern hemisphere so I will have to write to a "dead" website again, oh well here goes:

Does inflammation and subsequent erosion of the lower esophagus precede inflammation of the heart and subsequent fibrosis?

Basically, my first heart trouble started in 1983 when I had my first run of tachycardia. In the years to follow I had a few intermittent bouts of tachy culminating in a visit to a cardio in 1993. Nothing to worry about I was told. In 1997 I had my first afib attack.

Now the thing is something must have started to go wrong between the years 1983 and 1997. These years were also some of the most enjoyable in my life. Lots of partying, drinking, eating out, socialising at work, sport, traveling etc. You know, the things we have ALL done.
My esophagus must have copped a real hammering in these years.

So now to a theory.

From 1983 to 1997 the esophagus would have been under stress through bad diet and the LES would be gradually weakening under the strain. Inflammation and erosion and subsequent damage to the underlying vagus nerve must have been taking place.

The heart in this same period must have been trying to cope with an erratic and over stressed vagus nerve and an inflamed esophagus on the doorstep. The kidneys and endocrine system must have been stressed too so maybe there was extra aldosterone and what ever else to cope with as well.

So what does the heart do? It now has to overcome an erratic vagus nerve and the electrical interference that would entail. So the heart starts producing the extra specialised cells to cope with this electrical interference. A defence mechanism so to speak. (I don't know the name of the cells…the one's they ablate). Inflammation from the esophagus would also be gradually affecting the heart.

The erratic over stressed vagus nerve, the erratic electrical interference and inflammation in the esophagus, combined, would gradually cause atrial inflammation and enlargement. Gradually chaos and eventually bingo!!!! Atrial fibrillation.

Anyway, that's my go at this jigsaw puzzle in layman's terms. Maybe some of you medically minded people can help here? Back to work.

Dean

Dean,

Amazing. My first runs of palps in 1987. GERD kicked off BIGTIME in 1988 (had been around to a lesser extent previously). LOTS of partying and binge-drinking from errr.. 1978 to 2002 (first diagnosed AF episode in May02 - although with hindsight I know for certain I had a 3 hr one early one morning in Oct 99). 3 more AF episodes since the aforementioned 2 - Nov02, Oct03 & Nov03. (Funny how they mostly come in Autumn.... fingers crossed I can get thru this Autumn with a lot less boozing, a good K & Mg-rich largely organic diet & lots of fish/oil.)

Mike F.

Dean - I believe you have made the connection for your situation....and everything I read says anytime something irritates the vagus nerve, there will be problems....in our case...AF. We know the location of the vagus and what it innervates.

irritation = inflammation - anything with an "itis" indicates inflammation.. gastritis, esophagitis, etc.

In the hiatal hernia/vagus nerve article I cited a while back, it was clearly evident that the hyperexcitation of the vagus was a culprit.

Have you had your C-reactive protein measured. This is overall-systemic inflammation....could come from something as simple as a food allergy response.

If it's up, the answer is (to me) clearly that the vagus nerve will be hyper-irritated and we know what that does WRT AF.

Jackie

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PeggyM
