

THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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Editorial

The LAF survey is shaping up to be a major success – and a lot of work! More than 40 completed questionnaires have been returned and I am about halfway through the initial compilation of the answers. It is already clear that a thorough analysis of this almost overwhelming amount of data will not only help pinpoint the mechanisms behind LAF, but may ultimately help lead to a solution.

*In this issue of **The Afib Report** we will present some very preliminary findings from the survey and explain how antiarrhythmic drugs work and whether they are likely to be useful in the treatment of LAF.*

*Yours in health,
Hans Larsen*

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Preliminary Results from Survey

The typical afibber is a male college or university graduate in his early forties to late sixties who is involved in brain rather than physical work. Women also get LAF, but it would seem from our results anyway, at only 10% of the rate for men. Our typical afibber is generally healthy and fit, has no major illness other than LAF, and does not smoke. In other words a paragon of virtue. So why does he get saddled with this debilitating condition?

I originally thought that the increased stress of daily living was to blame, but the survey results show otherwise. There certainly are a few (10%?) afibbers where it is clear that the main cause of their problem is excessive stress. The

vast majority of respondents is, however, either retired or describe themselves as “laid-back” or “easy-going”. So why do they get afib attacks?

The majority of afibbers is highly athletic and has been so for most of their lives. It is ironic that the individuals who chose to follow the recommendations put forth in the 60s to exercise and “be vigorous” are now reaping the rewards of following this advice in the form of LAF. The survey clearly shows this and our preliminary findings are backed up by an earlier study done at the University of Helsinki[1]. This study done in 1998 concludes that men who engage in long-term vigorous exercise have a 5 times greater risk of developing LAF than do less active men. There are compensations though, vigorous exercisers have a 5 times lower overall mortality rate and a 3 times lower risk of developing coronary heart disease than do less active men. Again, our survey supports these findings. Not one respondent, so far, has indicated that he or she has diabetes and the incidence of high blood pressure is probably about 10% as compared to the expected rate of 40-50% for a comparable sample of non-afibbers.

Perhaps one of the most intriguing observations is that the majority of attacks (75%) happen in the period between 6 PM and 8 AM. Less than 20% occur between Noon and 6 PM and so far, only one respondent reports attacks between 8 AM and Noon. It is well known that the heart (pulse) rate is fastest at about 11:30 AM and slowest at about 2:30 AM. Actually the Chinese have been aware of this circadian variation in heart rhythm for the last 2000 years. Chinese medicine recognizes that the heart qi (energy) peaks between 11 AM and 1 PM and is at its lowest between 11 PM and 1 AM. So what has this got to do with the timing of LAF attacks, you may ask?

Actually everything! It is clear that the attacks happening when the heartbeat is fastest (in the morning) are adrenergic in nature while the attacks happening at night, at rest or during digestive periods are vagal in nature. It is also evident from our survey that athletic afibbers experience their attacks between 6 PM and 8 AM. Why? The Finnish study provides some clues. Highly athletic people have large hearts (physically that is) and slow heart beats. A daytime pulse rate of 50 is not uncommon. This means that at night or during digestive periods these highly athletic afibbers' heart rates can drop so low that a bradycardia (excessively slow heart rate) may develop. A bradycardia is a potentially serious condition so it is plausible that the autonomic control system will try to avoid it by invoking a response from the sympathetic (adrenergic) branch. If this response (release of norepinephrine from nerve endings) is a little too enthusiastic or engages foci of highly excitable cells in the atrium a LAF attack may follow. It is also possible that an excessive release of acetylcholine from the parasympathetic system in itself could initiate AF. Add to this evidence that large atria (hearts) are more likely to enter into afib and sustain it than are smaller ones and the scene is set for an exceptional vulnerability to LAF. Because women tend to have smaller and faster beating hearts they seem to be much less likely to develop vagally mediated LAF.

To summarize, attacks happening during the day (especially in the morning) are adrenergic in nature, usually initiated by physical or mental stress and involve an overactive sympathetic nervous system. Attacks that happen at night or at rest are vagally mediated and involve an overactive parasympathetic system most likely coupled with an over-enthusiastic reaction from the sympathetic branch. The distinction between the two forms cannot be over-emphasized. They have entirely different origins and mechanisms and require different treatment. This does not mean that the two forms cannot coexist in the same individual. A hard-driving, tense person who is a fanatic physical fitness enthusiast may have both types of attacks, but fortunately, as we shall see, this is not a very common condition.

So what is the answer to preventing LAF attacks? Many afibbers have been prescribed antiarrhythmic drugs so we shall begin by reviewing how these drugs work and the rationale for their use.

Antiarrhythmic Drugs: How They Work

The very first thing to realize is that no drug has ever been developed specifically for the treatment of LAF. All the antiarrhythmics available were expressly developed for the treatment of arrhythmias arising from cardiovascular disease and heart attacks. The second thing to bear in mind is that ALL arrhythmias connected with heart disease are adrenergic in nature. As a consequence there is very little research on the use of antiarrhythmics in the management of vagally mediated LAF.

Antiarrhythmic drugs are divided into 4 classes depending on their mode of action[2,3]. To understand how they work let us take a brief look at the modus operandi of an individual muscle cell (myocyte) in the heart. The membranes of myocytes act as small pumps that pump sodium, potassium and, to a lesser extent, calcium and magnesium ions in and out of the cells. When the cell is at rest the concentration of potassium is high inside the cell and the concentration of sodium is high outside the cell. At certain times the ion channels which allow entry of sodium into the cell open and sodium ions rush into the cell causing it to generate an electric charge (depolarization) and contract. The contractions proceed from cell to cell making the whole muscle fiber contract and ultimately making the whole atria contract.

Potassium leaks out of the cell during the depolarization period, but as soon as the depolarization is over it begins to flow back into the cell during what is called the rest or refractory period. Atrial fibrillation is

characterized by a total lack of refractory periods. Calcium and magnesium ions follow the sodium and potassium ions respectively, but at a slower rate. Thus sodium and calcium are “excitatory” ions while potassium and magnesium can be viewed as “calming” ions. This underscores the importance of having adequate intracellular levels of both potassium and magnesium and also explains why a magnesium infusion often halts AF. It is likely that a potassium infusion would have a similar effect, but it would be far too dangerous because of the much faster action of potassium ions.

The rate of the fibrillating heart can be slowed by partially blocking the ion channels that allow the influx of sodium or calcium or the outflow of potassium. Antiarrhythmic drugs owe their effectiveness to their capability to block ion channels. Class I drugs such as quinidine, disopyramide, flecainide and propafenone primarily block the sodium channels, but also have some potassium blocking effect. Class III drugs such as sotalol, amiodarone and dofetilide primarily block the potassium channels and class IV drugs such as verapamil and diltiazem block the inward movement of calcium. Class II drugs, the so-called beta-blockers, have no direct effect on the heart cells, but slow the heart rate by blunting the stimulatory effects of norepinephrine and the sympathetic nervous system.

This then is the arsenal available to the cardiologist and electrophysiologist in the battle against arrhythmias. Do they work? Yes and no! Some of them are highly effective in the treatment of life-threatening ventricular arrhythmias, but most of them are of little use when it comes to preventing LAF, particularly LAF of vagal origin.

Beta-blockers such as atenolol and propranolol, and antiarrhythmics like flecainide, propafenone, sotalol, amiodarone, verapamil, and diltiazem are the drugs most often prescribed for LAF. Digoxin (Lanoxin) used to be widely used, but has now been totally discredited. Several clinical trials have shown that it can lengthen attacks and even cause the LAF to become chronic[4]. Verapamil and diltiazem are useful in lowering the heart rate during an attack, but do not prevent attacks or speed up the conversion to sinus rhythm. Flecainide is useful in converting afib to sinus rhythm and somewhat useful in preventing attacks. It does, however, have some rather nasty side effects including sudden death. It, like other antiarrhythmic drugs, can also cause arrhythmias.

It is easy to see why drugs like flecainide have serious side effects. Their action is not limited to the atria. They also slow down the action of the ventricles – sometimes with disastrous results. Propafenone is somewhat similar to flecainide; however, it also has slight beta-blocking properties making it a poor choice for afibbers with vagal LAF. Sotalol is not effective in converting to normal sinus rhythm, but has some preventive action. It also has beta-blocking properties. Amiodarone is used in patients with serious ventricular arrhythmias and is generally not recommended for LAF due to its potentially devastating adverse effects. To quote the authors of the chapter on “Oral Antiarrhythmic Drugs Used for Atrial Fibrillation”[3], “The long-term efficacy of antiarrhythmic drugs for preventing a recurrence of AF is far from ideal”!!

Are these drugs useful at all in the management of LAF? The answer to this depends on what type of LAF you have. At present the adrenergic type is far easier to prevent than the vagal type.

Prevention of Adrenergic LAF

The simplest pharmaceutical method of preventing an adrenergic attack is by taking a small amount of beta-blocker (25 mg atenolol or 5 mg propranolol) when you feel an attack is imminent, before attending a stressful meeting or in general, when you know you are likely to be exposed to excessive stress. Since beta-blockers may promote vagal attacks it is best not to take them too late in the day so as to minimize the risk of a vagal attack later in the evening when vagal tone is higher.

Many doctors recommend taking 25 or 50 mg of atenolol (or the corresponding amount of propranolol) twice a day. This is probably a less than sterling idea unless you have been diagnosed with hypertension. Continuous use of beta-blockers lowers blood pressure and heart rate significantly leading to fatigue and an increased risk of vagal attacks. Getting off beta-blockers after continuous use can also be a problem as the blood pressure may rise precipitously when the drug is discontinued.

I have personally found that an 8-oz. glass of fresh, organic celery juice sipped slowly is just as effective in preventing a LAF attack as is 25 mg of atenolol.

Beta-blockers (and verapamil) can also be used to slow the heart rate during an attack. They do not speed up the conversion to normal sinus rhythm. Conversion to sinus rhythm usually occurs spontaneously within the first 48 hours. Cardioversion is sometimes effective in converting episodes of longer duration, but for some unknown reason afibbers who have been cardioverted don't stay in sinus rhythm for very long. Flecainide and propafenone are usually effective in converting to normal sinus rhythm within a few hours. They can also be effective in preventing further episodes of an adrenergic nature. However, they are both highly dangerous drugs and their use should be closely supervised by a cardiologist.

Whether you should use flecainide or propafenone on a continuous basis depends to a large extent on how often you have episodes. If just a few times a year it is probably best to just use them when needed to convert quickly – this approach would eliminate a lot of nasty, long-term side effects. On the other hand, if attacks come on every second day or every week continuous use may be indicated – assuming that celery juice and beta-blockers do not do the trick. Sotalol is another possible choice, but from all accounts the side effects are pretty bad so I would approach this drug with caution. Finally, flecainide, propafenone, sotalol, and amiodarone all share the dubious distinction of having killed more people than placebo in the clinical trials that evaluated them.

I do believe I am running out of space – and time. Next month I will discuss the pharmacological treatment options for vagal LAF and carry on with the reporting of the survey results. Also, in the next and future issues I will focus on the non-pharmacological options for the management of LAF. Yoga, qi gong, deep breathing, meditation, and certain traditional Chinese medicine approaches may well prove to be the ultimate solution. It is also possible that certain herbal combinations could be effective in preventing vagal attacks.

Until next month!

References

1. Karjalainen, Jouko, et al. Lone atrial fibrillation in vigorously exercising middle aged men: case-control study. *British Medical Journal*, Vol. 316, June 13, 1998, pp. 1784-85
2. Falk, Rodney H. and Podrid, Philip J., editors. *Atrial Fibrillation: Mechanisms and Management*. 2nd edition, 1997, Lippincott-Raven Publishers, Philadelphia, PA.
3. Saoudi, Nadir, et al., editors. *Atrial Flutter and Fibrillation: From Basic to Clinical Applications*. 1998, Futura Publishing Co., Armonk, NY.
4. Sticherling, Christian, et al. Effects of digoxin on acute, atrial fibrillation: induced changes in atrial refractoriness. *Circulation*, Vol. 102, November 14, 2000, pp. 2503-08

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