

THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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Editorial

In this issue we report on the effectiveness of antiarrhythmic drugs as determined from our recent surveys. Not surprisingly, the only drugs that showed any appreciable benefit were flecainide (Tambocor) and disopyramide (Norpace) when used by vagal afibbers. Metoprolol (Toprol, Lopressor) was somewhat effective for adrenergic and mixed afibbers either on its own or in combination with flecainide or disopyramide. Digoxin (Lanoxin) and sotalol (Betapace) turned out to be totally useless for preventing episodes in paroxysmal afibbers and among other side effects clearly promoted palpitations and atrial fibrillation. A very poor choice indeed! Amiodarone has benefited some afibbers, but its horrendous side effects rule it out as a viable drug for a non-life threatening condition such as LAF.

The research report this month investigates the connection between stress and lone atrial fibrillation with particular emphasis on a possible connection between LAF and cortisol levels. We also explore the association between cortisol levels and diet and lifestyle.

Enjoy!

*Yours in health and sinus rhythm,
Hans Larsen*

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(vagal, adrenergic, and mixed) and by major subgroup of drugs.

Second, I have compiled and evaluated 211 responses regarding the effectiveness of individual drugs by the 115 respondents who had tried them. Most afibbers have tried several drugs thus there are many more individual responses than there are actual respondents.

Findings from LAFS II – Part 3

A. Effect of Antiarrhythmic Drugs

I have taken a two-pronged approach in evaluating the effectiveness of antiarrhythmics and beta and calcium channel blockers. First, I have compared the overall episode frequency and duration in afibbers taking these drugs with the frequency and duration among afibbers not taking drugs. This comparison is further stratified by type of afib

I believe this subjective evaluation of drug effectiveness is extremely revealing and worthwhile. The individual afibber is, by far, the best judge of what works and what doesn't. If a drug reduces the frequency or duration of episodes without significant side effects then the afibber will declare it a success and be keen to continue on it. If, on the other hand, the drug does not produce noticeable benefits or has horrendous side effects then the afibber trying it will get off it and declare it a failure.

Before we get into the actual evaluation it may be worthwhile to just briefly recap the properties and mode of action of the drugs evaluated.

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. 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.

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. 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 supposedly 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.

Use Versus Episode Frequency and Duration

A total of 179 respondents submitted data concerning drug use and episode severity. Of the 148 paroxysmal afibbers 77 had the vagal variety, 20 the adrenergic, and the remaining 51 the mixed form of LAF. Thirty-one were in chronic afib; these respondents are omitted from the following evaluation as drugs would clearly not

affect the frequency and duration of episodes although they may affect their heart rate and general feeling of well-being.

Eighty-seven (59%) of the paroxysmal afibbers were currently using a pharmaceutical drug to ward off or shorten episodes while 61 (41%) were not taking any such drugs. The average number of episodes over a six-month period was 11 for drug takers and 8 for non-drug takers; this difference was not statistically significant.

The average duration of an episode was 9 hours for both drug takers and non-drug takers and there was no significant difference in the total time spent in fibrillation over the six-month survey period (79 hours versus 75 hours).

There were no differences between drug takers and non-drug takers as far as average age, gender distribution or total years of LAF. The finding that, overall, afibbers who take antiarrhythmics are no better off than afibbers who do not is indeed surprising; however, it should be kept firmly in mind that none of the drugs prescribed for LAF have been specifically developed to deal with this condition and, as a matter of fact, some of them are not even approved for the treatment of paroxysmal atrial fibrillation as such. So essentially whenever a LAF patient is prescribed an antiarrhythmic it is a trial and error procedure – there is no guarantee of success. This is compounded by the fact that many afibbers are clearly receiving the wrong drugs for their particular condition. This is particularly pronounced among vagal afibbers.

Drugs in Vagal LAF

Forty-eight of the 77 vagal afibbers (62%) were taking antiarrhythmics or other drugs to prevent or ameliorate episodes. The average number of episodes over a six-month period was 12 for drug takers and 10 for non-drug takers. The average duration of an episode for drug takers was 9 hours as compared to 11 hours for those not on drugs. None of these differences were statistically significant.

A closer look at the collected data shows that the seeming overall lack of effect of drugs is actually caused by the fact that some drug takers are on drugs that are clearly contraindicated for their condition while others are on drugs that are beneficial. There is ample evidence that vagal afibbers should not take digoxin (Lanoxin), beta-blockers or antiarrhythmics with beta-blocking properties as these drugs are known to markedly worsen their condition. Yet, of the 48 vagal afibbers on drugs 24 (50%) were on beta-blockers or drugs with beta-blocking properties. These people had an average of 9 episodes lasting 12 hours over the six-month survey period. In comparison, vagal afibbers on the drugs best suited for them flecainide (Tambocor) or disopyramide (Norpace, Rythmodan) had 17 episodes lasting an average of only 4 hours over the survey period. Vagal afibbers on contraindicated drugs spent an average of 106 hours in afib over the period as compared to 41 hours for those on flecainide or disopyramide and 116 hours for those taking no drugs at all. The number of afibbers having no episodes at all was 7 (41%) in the flecainide/disopyramide group, 3 (12%) in the beta-blocking group, 1 (17%) in the group on a variety of other drugs, and 7 (24%) in the group taking no drugs.

The conclusion from this data is that vagal afibbers who cannot tolerate flecainide or disopyramide are better off taking no drugs at all.

Drugs in Adrenergic LAF

Eleven of the 20 adrenergic afibbers, for which complete data is available, took drugs while 9 (45%) did not. Afibbers on drugs had an average of 2 episodes over the six months while those not on drugs had 6. The duration of episodes was 13 and 17 hours respectively. Although these differences were not statistically significant due to the small sample size, there is a trend for some drugs to be beneficial for adrenergic afibbers. The most successful would appear to be metoprolol (Lopressor, Toprol).

Drugs in Mixed LAF

Twenty-eight (55%) of the 51 mixed afibbers took drugs while the remaining 23 (45%) did not. Those on drugs had an average of 15 episodes lasting 9 hours during the six months as compared to 7 episodes lasting 5 hours for the non-drug group. Overall, the drug group spent an average 107 hours in afib over the period compared to 29 hours for the non-drug group. This difference is statistically significant ($p=0.04$) and indicates that mixed afibbers may be better off not taking any drugs. This finding is perhaps not too surprising as most of the drug group were taking drugs (beta-blocking), which would aggravate the vagal component of their condition.

Drugs in Chronic LAF

Eleven (35%) of chronic afibbers took no drugs while the remaining 20 were on a variety of beta-blockers and other drugs. Most popular were amiodarone (5 respondents), diltiazem (5 respondents), verapamil (3 respondents), sotalol (2 respondents), and flecainide (2 respondents). It is not immediately clear why some chronic afibbers are on antiarrhythmics (amiodarone, sotalol, flecainide) as there is no evidence that this will help them convert to sinus rhythm unless they are being prepared for cardioversion – none of these respondents were. It would make more sense just to take diltiazem or verapamil to keep the heart rate under control and avoid highly dangerous drugs like amiodarone and flecainide.

In conclusion, the data collected in the survey does not support the assumption that treatment with antiarrhythmics is generally beneficial to people with lone atrial fibrillation. There are clearly cases where afibbers have been helped by these drugs, e.g. flecainide or disopyramide for vagal afibbers, but in general terms they do not seem to be helpful and, in many cases, are clearly detrimental. It would appear to be up to each individual, in cooperation with his or her physician, to find the right drug or to forego antiarrhythmics altogether. Remember that LAF is not life-threatening, but antiarrhythmics can be. The best and safest approach for many afibbers may well be to just take verapamil or diltiazem during an episode to keep the heart rate under control.

B. Subjective Evaluation of Drug Performance

A total of 115 respondents reported on the various drugs they had tried and provided their judgment as to which ones were beneficial and what side effects were observed. The results are as follows:

Atenolol (Tenormin)

A total of 22 afibbers (7 vagal, 7 adrenergic, 7 mixed and 1 chronic) had tried atenolol. None of the vagal afibbers had found it beneficial when taken continuously, but one respondent had found it useful to take periodically when under stress. Only 2 out of 7 adrenergic afibbers had found it useful with one entering a “maybe”. Again, only 2 of the mixed afibbers had found it useful while the remaining 5 had not. One chronic afibber thought that it may be beneficial. Thirteen of the atenolol users (59%) reported one or more side effects with fatigue being reported by 7 respondents, slow heart rate and low blood pressure by 4, and dizziness by 3. The most common dosage was 25 mg once a day with a range of 12.5 to 100 mg/day. Overall benefit rate with daily use of atenolol was 0% for vagal and 29% each for adrenergic and mixed afibbers.

Metoprolol (Toprol, Lopressor)

A total of 21 afibbers (11 vagal, 5 adrenergic and 5 mixed) had tried metoprolol. None of the vagal afibbers had found it beneficial. Two of the adrenergic afibbers had found it beneficial, 2 had not, and 1 had entered a “maybe”. Four mixed afibbers had found metoprolol useful while 1 had not. Fifteen (71%) of users reported side effects with fatigue being reported by 7 respondents and slow heart rate and low blood pressure reported by 4. The most common dosages were 25 or 50 mg once or twice a day, but 2 respondents took 200 mg/day. Overall benefit rate with daily use of metoprolol was 0% for vagal, 40% for adrenergic, and 80% for mixed afibbers.

Other beta-blockers (bisoprolol, propranolol)

Four afibbers (3 vagal and 1 adrenergic) had tried bisoprolol or propranolol. None had found these beta-blockers beneficial, but one vagal afibber had entered a “maybe”. Two of the respondents reported fatigue as a side effect. Overall benefit rate with daily use of bisoprolol or propranolol was 0% for both vagal and adrenergic afibbers. Please note this conclusion is based on data from only 3 afibbers.

Amiodarone (Cordarone, Pacerone)

Seventeen afibbers (8 vagal, 1 adrenergic, 4 mixed and 4 chronic) had tried amiodarone. Four vagal afibbers had found it beneficial while 4 had not. One adrenergic had found it beneficial, but none of the 4 mixed afibbers had done so. Two (50%) of the chronic afibbers had found amiodarone to be of no benefit while 1 had found it beneficial and one was not sure. Ten users (59%) reported side effects with thyrotoxicosis being experienced by 5 users. The most common dosage was 200 mg once a day. Overall benefit rate with daily use of amiodarone was 50% for vagal, 100% for adrenergic, 0% for mixed, and 25% for chronic afibbers.

Disopyramide (Norpace, Rythmodan)

Eight afibbers (5 vagal and 3 mixed) had tried disopyramide. Four (80%) of vagal and 2 (67%) of mixed afibbers had found the drug beneficial. The most common side effects were urinary problems and dry mouth, which was experienced by 38% of all afibbers taking disopyramide. Overall benefit rate with daily use was 80% for vagal and 67% for mixed afibbers.

Flecainide (Tambocor)

Twenty-six (19 vagal, 1 adrenergic and 6 mixed) had tried flecainide. Twelve (63%) of vagal afibbers had found it beneficial while 6 (32%) had not. The lone adrenergic respondent had not found it beneficial, but 4 out of 6 (67%) of mixed afibbers had. Twelve (46%) of all users reported side effects with fatigue being the most common. The most common dosage was 100 mg twice a day ranging from 50 mg to 300 mg/day. Overall benefit rate was 63% for vagal, 0% for adrenergic, and 67% for mixed afibbers.

Propafenone (Rythmol)

Nineteen (8 vagal, 2 adrenergic, 7 mixed and 2 chronic) afibbers had tried propafenone. Three (38%) of vagal afibbers, one (50%) of adrenergic, and 2 (29%) of mixed had found it beneficial. The 2 chronic ones were not sure about the benefits. Nine (47%) of all users reported side effects with fatigue being the most common. The most common dosage was 150 or 225 mg 3 times a day ranging from 100 mg to 300 mg 3 times a day. Overall benefit rate was 38% for vagal, 50% for adrenergic, and 29% for mixed afibbers.

Sotalol (Betapace, Sotacor)

Thirty-eight (22 vagal, 3 adrenergic, 11 mixed and 2 chronic) afibbers had tried sotalol. Not one (0%) had found it beneficial although one vagal afibber thought it might have reduced severity, but not frequency of episodes. Twenty-nine (76%) of all users reported side effects with 11 actually reporting heart palpitations or fibrillation as the main side effect. Another 7 reported increased fatigue. The most common dosage was 80 mg twice a day. With a success rate of 0% and side effects occurring in 76% of users sotalol is easily classified as the most useless drug for lone afib. Unfortunately, it is the most frequently prescribed one.

Digoxin (Lanoxin)

Twenty-two (12 vagal, 1 adrenergic and 9 mixed) afibbers had tried digoxin. Only 1 mixed afibber had found it useful in keeping heart rate under control. The remaining 21 (95%) had found no benefits from taking the drug. Seventeen (77%) of all users reported side effects with the most common being palpitations and atrial fibrillation (32%) and fatigue (23%). The most common dosage was 0.25 mg daily. With only one respondent out of 22 finding some benefit from digoxin and 77% experiencing serious side effects digoxin clearly ranks right alongside sotalol as the most useless drug for LAF.

Diltiazem (Cardizem, Tiazac)

Eleven (5 vagal, 1 adrenergic, 2 mixed and 3 chronic) afibbers reported that they had tried diltiazem. None of the paroxysmal afibbers had found it useful in preventing episodes. The 3 chronic afibbers were not sure if it had been beneficial. Five users (45%) reported unspecified side effects. The most common dosage was 240 mg once a day. While it is not surprising that diltiazem was not found to prevent episodes it is somewhat surprising that nobody found it beneficial in other ways (keeping heart rate down).

Verapamil (Veramil)

Twelve (6 vagal, 1 adrenergic, 3 mixed and 1 chronic) afibbers had tried verapamil. Only 1 vagal, 1 mixed and 1 chronic afibber had found it beneficial in reducing symptoms (not frequency) of episodes. Eight (67%) users reported side effects with fatigue being the most common. Most common dosage was 240 mg once a day, but dosages of 80 mg 4 times a day and 120 mg once a day were also reported.

Drug combinations

Five afibbers had tried a combination of flecainide and a beta-blocker or calcium channel blocker. One mixed afibber had found this combination beneficial [using 100 mg/day flecainide and 10 mg/day propranolol (Inderal)] and one vagal afibber had found a combination of 200 mg/day of flecainide and 10 mg/day of nadolol to be of benefit. The remaining 3 had found no benefit of the combinations although one mixed afibber on 50 mg flecainide and 50 mg atenolol twice daily thought it might be somewhat beneficial. Side effects were few.

Three afibbers had tried a combination of propafenone and beta-blockers. One adrenergic afibber had found a combination of 150 mg propafenone and 50 mg metoprolol twice a day to be beneficial. The other 2 found no benefits.

One mixed afibber had found a combination of 25 mg metoprolol and .125 mg digoxin daily to be of benefit.

Drugs for conversion only

One vagal afibber has found that taking 225 mg of propafenone at the beginning of an episode helps speed up conversion – usually converts within a few hours. One mixed afibber has found that taking flecainide at the onset of an episode speeds up conversion. Both of these findings are in accordance with the results of clinical trials aimed at testing the efficacy of flecainide and propafenone for conversion.

Conclusion

It is clear that the most effective drugs for vagal afib are flecainide and disopyramide. Although not terribly effective the best drugs for adrenergic afibbers would appear to be metoprolol and propafenone either singly or in combination. Mixed afibbers may do well on metoprolol with flecainide and disopyramide either singly or in combination with metoprolol also showing some effectiveness. No drug except perhaps verapamil was deemed to be of benefit for chronic afibbers. Sotalol and digoxin are totally useless and have serious side effects. Amiodarone has been beneficial to some afibbers, but its terrible side effects rule it out as a viable drug for a non-life threatening conditions such as LAF.

Although the above conclusions are based on subjective evaluations by 115 afibbers they are in remarkably good agreement with clinical experience and with the conclusions reached by relating actual episode severity to drug use. I believe these conclusions can be used as guidelines if you want to try a drug to reduce the number or duration of LAF episodes. Bear in mind though that both flecainide and disopyramide are very powerful and should only be used by afibbers with structurally sound hearts; they also tend to lose their effectiveness over time.

Finally, do keep in mind that 40% of all afibbers participating in our survey use no drugs to prevent episodes and, on aggregate, have no more episodes than do afibbers on drugs. Whether or not drugs help is clearly a highly individual matter and much experimentation will likely be required to find the optimum one for you – if indeed there is one.

C. Follow-up on Ablation Procedures

In the May issue we reported on the results of 15 ablation procedures. Four had been completely successful, 4 were clearly not successful, and 6 were done so recently (November 2001 – January 2002) that it was too early to tell whether they had been successful or not. One of the respondents was still on beta-blockers after the operation.

We have now followed up on the recently performed procedures and can report that we have heard from 4 of the afibbers who underwent ablation therapy late last year or early this year. Three of the procedures were completely successful and one was not. This brings the final score to:

- Vagal – 4 successful; 3 not
- Adrenergic – No procedures done
- Mixed – 2 successful; 3 not
- Chronic – 1 successful; 1 not

The successful procedures were done at the Cleveland Clinic (3), Presbyterian Hospital (1), Duke Medical Center (1), and Virginia Mason in Seattle (1).

That's it for now. In the next issue we will discuss the benefits of supplements and relaxation therapies.

The Stress Connection

Stress (emotional or physical) is the single-most common trigger for afib episodes. It is particularly significant for adrenergic and mixed afibbers with over 90% of adrenergic and 56% of mixed afibbers listing emotional or work-related stress as an important trigger[1].

Stress is the body's response to an event that upsets its normal balance (homeostasis). Stressors can be physical, emotional, chemical or biological. Examples of physical stressors are vigorous exercise, trauma, exposure to cold, and surgery. The most common chemical stressor, apart from adverse drug and food reactions, is hypoglycemia (low blood sugar). Emotional stressors run the gamut from anxiety to depression, fear of flying, an exam or other difficult mental task, fear of demotion or loss of job, marriage break-up, loss of a loved one, moving house, etc. In short, it can be anything that taxes you emotionally or gives you a gut feeling that something is not right. Bacterial and viral infections and fever are the most common biological stressors[2-5]. Stress can be acute, like when you face a mugger in a dark alley or chronic, like when you have to deal with an unreasonable boss every day.

The Body's Reaction to Stress

The body has one basic response to all types of stress – it releases stress hormones. In the case of acute stress adrenaline (epinephrine) is released giving rise to the so-called “fight or flight” reaction. In the case of chronic or long-term stress the body releases cortisol or at least attempts to do so. There is some overlap as to which hormones are released when, but generally adrenaline is released in response to short-term (acute) stress whilst cortisol is released in response to long-term (chronic) stress.

While it is clear that the fight or flight reaction caused by adrenaline release can be life-saving it is not entirely clear why the release of cortisol would help protect against the effects of long-term stress[2]. There are two major physiological effects of cortisol release – a rise in blood glucose levels and an anti-inflammatory effect[2]. Release of adrenaline also causes a rise in glucose levels. This is of particular importance when it comes to rapidly reversing the effects of hypoglycemia (low blood sugar).

The Glucose Connection

Glucose (sugar) is the body's main energy source and is particularly important for fuelling the brain. Glucose gets into the blood through consumption of sugar or sugar-containing foods or via the breakdown of carbohydrates into simple sugars. Insulin (produced in the pancreas) is a chemical messenger that acts on the walls of the cells to cause the release, from within the cell, of special protein molecules – the so-called GLUT-4 transporters. The GLUT-4 transporters rise to the cells' outer membranes where they grab hold of the glucose molecule and transport it into the interior of the cell where it is used to produce energy. Excess glucose is stored as fat or converted to glycogen, which is stored in the liver and muscles.

Blood levels of glucose are controlled within narrow limits by the counter-regulatory actions of insulin and glucagon (also produced in the pancreas). Insulin is released in response to a carbohydrate meal and glucagon (and some insulin) is released in response to a protein meal. If glucose levels fall too low in between meals glucagon will act on the glycogen stored in the liver and muscles and initiate the release of glucose into the blood stream. However, if only high carbohydrate meals are consumed there may not be enough glucagon to do the job and the body will then alert the back-up system. This causes the release of cortisol or, in extreme cases, adrenaline in order to bring the glucose levels up by converting glycogen stored in the liver[6]. In other words, cortisol can be released not only by exposure to a stressor, but also directly in response to low glucose levels caused by an inadequate glucagon supply.

When it comes to glucose the brain is a very strict taskmaster indeed. It will not tolerate low glucose levels for very long before it hits the “panic button”. It is also clear that the brain is pro-active, that is, it reacts to any stressor by demanding more glucose as a precaution. This demand is met by the release of stress hormones.

The Ins and Outs of Cortisol

Unless you are on a battlefield or in an inner city at night and are exposed to high levels of acute stress it is likely that cortisol rather than adrenaline will be released to preserve or increase glucose levels during stress. The

release of cortisol is initiated in the hypothalamus region of the brain. This region receives input concerning physical and psychological stressors acting on the body and if they cannot be dealt with by the central or autonomic nervous system the hypothalamus initiates the release of stress hormones. Corticotropin-releasing hormone (CRH) is produced in the hypothalamus in order to carry a message to the pituitary gland to produce and release adrenocorticotrophic hormone (ACTH) that, in turn, is carried in the blood stream to the outer parts of the adrenal glands. The outer part (cortex) of the adrenal glands initiates the manufacture of cortisol, which upon entering the blood stream proceeds to the liver and causes the release of glucose. The cortex also produces dehydroepiandrosterone (DHEA) and testosterone. All three hormones are derived from the precursor pregnenolone and actually competes for "the right" to use up pregnenolone[2,3,5]. So if the priority is cortisol production then there is not much pregnenolone left over for producing DHEA and testosterone. In other words, long-term stress can play havoc with your sex life and reduce your DHEA levels.

Cortisol levels, in non-stress conditions, are normally tightly controlled and follow a predictable diurnal pattern with levels being highest just after awakening and declining during the day to reach their lowest level during the night. Both excessively high and excessively low cortisol levels can have devastating effects. Addison's disease is the result of a cortisol deficiency whereas Cushing's disease is associated with consistently excessive levels. Adrenal exhaustion is seen after prolonged exposure to stress[2,3,5].

High cortisol levels have also been implicated in irritable bowel syndrome, anorexia, and osteoporosis[7-10]. It is interesting that women with a history of childhood abuse are extremely sensitive to stress in later life and release much greater amounts of ACTH than do women who have experienced a normal childhood[11]. This could indicate that the body is trying to get the adrenals to produce cortisol (by releasing ACTH) but that they are too exhausted to respond. Although only women were evaluated in this study another study found that children of both sexes who had experienced a traumatic childhood (family fights or abandonment) had consistently higher cortisol levels than did children in more harmonious families[12]. These higher than normal childhood cortisol levels could lead to adrenal exhaustion and the inability to cope with stress in later life[12,13].

While there is ample evidence that high adrenaline levels can trigger and sustain atrial fibrillation there is practically none concerning the association between cortisol levels and AF. In searching the more than 11 million articles in MEDLINE I only came up with one dealing with the subject. This was published in the Russian heart journal "Kardiologija" in 1975. The researchers concluded that there is a distinct increase in cortisol excretion during an AF episode[14]. Could cortisol be triggering or sustaining atrial fibrillation? I have not come across any evidence to suggest this, not because it isn't so, but strictly because nobody seems to have looked into this possibility.

Clearly more research is required in this field and one good first step would be for a number of afibbers to obtain a salivary cortisol profile to see whether it is abnormal during sinus rhythm. I am having mine tested shortly and will let you know the results. In the meantime, I am endeavouring to keep my cortisol levels under control.

Managing Cortisol Levels

The inappropriate release of cortisol between meals can be avoided by eating frequent small meals and ensuring that each meal or snack contains protein, fat and carbohydrates. The idea behind using the diet as a tool for cortisol control makes imminent sense and is described in considerable detail in two recent books[15,16]. The same dietary approach is also effective for helping type 2 diabetics control their glucose levels.

It is interesting that some afibbers have been able to, at least partially, prevent episodes by dietary changes. One of the approaches involved eating a lot of chicken (mainly protein and fat); this may be helpful in keeping cortisol under control, but is probably not desirable for the long term. Other afibbers have found a correlation between episodes and saliva or urine acidity (pH) and have noted improvement by adjusting the diet to produce a more alkaline environment. A more alkaline environment is known to be associated with lower cortisol levels, but much more research is required to determine the optimum pH and how to achieve and maintain it[17].

Could dietary adjustments help control atrial fibrillation through cortisol control? There certainly are some tantalizing indications that it could, but more research is obviously required.

Another fairly simple way to manage cortisol levels is by going easy on the exercise. There is growing evidence that marathon running and other vigorous, sustained activities really are not beneficial and this applies doubly to afibbers. Any exercise lasting more than about 40 minutes sharply elevates cortisol levels and increases oxidative stress to the point that it becomes counterproductive[18,19]. Dr. Kenneth Cooper, MD, the “father of aerobics”, has reached the conclusion that too much exercise may actually increase the risk of developing medical problems[19]. It can also put a serious damper on your sex life by decreasing testosterone levels[19]. Most health experts now agree that one or two brisk 30-minute walks a day is the optimum exercise for staying healthy[20,21].

Several supplements have been found useful in keeping stress and cortisol levels under control. Among them vitamin C, the B vitamin complex, and phosphatidylserine[22-24].

Smoking and alcohol consumption both increase cortisol levels so should be avoided[25,26]. Meditation, visualization, deep breathing, listening to relaxing music, and especially, laughing a lot are all excellent ways of keeping cortisol levels under control as is having a warm, but not hot, bath (100-102 degrees F). As a matter of fact, using any of these methods to stop the initial adrenaline rush occurring at the beginning of an afib episode and then following up with a brisk walk to “burn-off” any remaining excess adrenaline and noradrenaline (norepinephrine) may well be an effective way of speeding conversion to sinus rhythm.

Can Cortisol Levels be Too Low?

A few years ago it was generally agreed that a high heart rate variability was beneficial whilst a low one warned of a possible early death from heart disease[27]. However, it is now clear that too high a heart rate variability is also detrimental; in other words, there is an optimum range where the risk of heart disease is minimized[28]. Could the same be the case for cortisol levels?

Indeed it could, excessively low cortisol levels may indicate adrenal exhaustion and result in increased ACTH excretion and an excessive reaction to short-term stress – not a good thing for afibbers. Researchers at the University of Minnesota recently found that adverse conditions that produced frequent elevated cortisol levels in childhood may contribute to low levels in adulthood and that these low levels may make the adult hypersensitive to stress. They conclude that lower than expected cortisol values should not necessarily be relegated to the file drawer because they contradict the current dogma that stress is only associated with high levels of cortisol[13].

Low cortisol levels or adrenal exhaustion have been associated with such diverse conditions as chronic fatigue syndrome, fibromyalgia, and rheumatoid arthritis[29-31]. Could lower than normal cortisol levels be a trigger for AF episodes? I am not aware of any research into this, but it is clearly a possibility. It is also a possibility that abnormal cortisol levels may affect adrenergic and vagal afibbers differently and that excessive ACTH or CHR levels could play a role in initiating or sustaining afib, but again, to my knowledge nobody has ever looked into this.

Conclusion

It is abundantly clear that medical research has not even scratched the surface concerning a possible association between atrial fibrillation and cortisol levels. Much remains to be discovered, but in the meantime having a cortisol/DHEA profile done may well prove worthwhile. Excessively high cortisol levels can be kept under control through dietary modifications and other relatively simple means and certain herbs and natural supplements will do much to relieve adrenal exhaustion. More about this in a future issue of The AFIB Report.

You may wish to wait for my results before proceeding, but if you do decide to have a cortisol/DHEA profile done (when in normal sinus rhythm) I would suggest that you ask your physician to order the “Adrenocortex Stress Profile” from the Great Smokies Diagnostic Laboratory in Asheville, NC. It will be much easier to compare results if we all use the same test and laboratory. Great Smokies has a good reputation for accuracy and reliability. You can find out more about the test at <http://www.gsdl.com/assessments/adrenocortex/>.

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