

The role of digoxin

1. What is the role of digoxin?

Question submitted by Dr. Atma Wadhwa, Sturgeon Falls, Ontario

Digoxin is probably the second oldest cardiac drug. Despite the number of years that we have been using it, we still don't seem to know its place in the therapeutic drawer.

Digoxin has come from being the panacea, where it was used for everyone with heart disease, to the villain, where leading cardiologists recommended that it never be used. And now, the pendulum has swung back, so that we now accept the fact that there clearly is a role for digoxin in managing our patients with atrial fibrillation (AF) and left ventricular (LV) dysfunction.

Digoxin is clearly indicated for the management of AF for rate control; this is particularly true for patients with LV systolic dysfunction. It is also indicated for LV systolic dysfunction as a third- or fourth-line agent when the maximum tolerated dose of angiotensin-converting enzyme

inhibitors, or angiotensin receptor blockers, β -blockers and diuretics are insufficient to adequately control symptoms of heart failure. In this setting, digoxin has been shown to reduce hospitalizations, but has not been shown to reduce mortality.

There are many problems in choosing a dose for a drug such as digoxin. These include:

- narrow therapeutic index,
- difficult to define therapeutic endpoints,
- inter- and intra-patient variability and
- varying effects of pathological states and drugs on digoxin's disposition.

In practice, the digoxin dose has been generally titrated according to the patient's:

- age,
- lean body weight and
- renal function.

Therapy is generally initiated at a dose of 0.25 mg q.d. in patients < 70 years of age, with good renal function. For those > 70 years of age with impaired renal function, a dose of 0.125 mg q.d. will suffice and a dose of 0.0625 mg is recommended for patients with marked renal impairment.

Answered by:

J. Wayne Warnica, FRCPC
 Professor
 University of Calgary
 Director
 Cardiac Intensive Care Unit
 Foothills Medical Centre
 Calgary, Alberta

We now accept the fact that there clearly is a role for digoxin in managing our patients with atrial fibrillation (AF) and left ventricular (LV) dysfunction

Using amiodarone

2. Amiodarone is used, at times, in the treatment of AF. What are the indications for its use in this condition? Why use it, if apparently, it does not alter mortality endpoints? And, when should one stop the use of it in someone who has had it prescribed to them?

Question submitted by Dr. Tom Bell, Peterborough, Ontario

One of the indications of amiodarone is the prevention of incidence of post-operative atrial fibrillation (AF) among high-risk patients following open heart surgery. The occurrence of AF in this situation is significantly reduced by a prophylactic amiodarone treatment.¹

Although outcomes such as death and stroke were not reduced by antiarrhythmic therapy in the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study² and the Rate Control vs. Electrical Cardio-version for Atrial Fibrillation (RACE) study,³ there are still many patients who remain highly symptomatic during AF, for whom rhythm control provides dramatic symptomatic benefit.

Amiodarone has been shown to be more effective than some other antiarrhythmic

therapies in maintaining sinus rhythm (Canadian Trial of Atrial Fibrillation Investigators [CTAFI])⁴ and so, the rhythm control strategy using amiodarone continues to be a reasonable alternative in such patients.

Like any other therapy, the decision to stop therapy should take into account the risks vs. the potential benefits. This must be an individual decision based upon the symptomatic response to therapy.

References

1. Budeus M, Hennersdorf M, Perings S, et al: Amiodarone prophylaxis for atrial fibrillation of high-risk patients after coronary bypass grafting: A prospective, double-blinded, placebo-controlled, randomized study. *Eur Heart J* 2006; 27(13):1584-91.

2. Wyse DG, Waldo AL, DiMarco JP, et al: A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002; 347(23):1825-33.
3. Van Gelder IC, Hagens VE, Bosker HA, et al: A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002; 347(23):1834-40.
4. Roy D, Talajic M, Dorian P, et al: Amiodarone to prevent recurrence of atrial fibrillation: Canadian Trial of Atrial Fibrillation Investigators. *N Engl J Med* 2000; 342(13): 913-20.

Answered by:

**J.G. Fodor, MD, PhD,
FRCPC**
Professor of Medicine
Head of Research
Prevention and Rehabilitation
Centre
University of Ottawa Heart
Institute
Ottawa, Ontario

Diet, exercise & cardiovascular disease

3. Do diet and exercise provide as much or more benefit than statins for cardiovascular disease?

Question submitted by Dr. F. Hossenbux, Ottawa, Ontario

In real-life situations, nutritional counselling has minimal effect on one's blood-cholesterol level. A meta-analysis of 19 randomized trials (RTs) studying the efficacy of dietary counselling showed a mean reduction in total cholesterol of 3%.¹ Another meta-analysis of 16 RTs did not find any effect of dietary interventions on overall mortality.²

Low level of physical activity is an independent risk factor for coronary heart disease (CHD). Increased level of physical activity:

- improves the feeling of well being,
 - leads to a reduction in blood levels of triglycerides,

- increases HDL-cholesterol and
- has a favorable impact on diabetes.

Unfortunately, hard evidence that increased physical activity will lead to a reduction in CHD events, or overall mortality, is so far missing.

Statins provide, incomparably, more benefit in CHD prevention than diet or exercise.

Answered by:

J.G. Fodor, MD, PhD, FRCP

Professor of Medicine
Head of Research
Prevention and Rehabilitation
Centre
University of Ottawa Heart
Institute
Ottawa, Ontario

References

1. Tang JL, Armitage JM, Lancaster T, et al: Systematic review of dietary intervention trials to lower blood total cholesterol in free-living subjects. *BMJ* 1998; 316(7139): 1213-20.
2. Studer M, Briel M, Leimenstoll B, et al: Effect of different anti-lipidemic agents and diets on mortality: A systematic review. *Arch Int Med* 2005; 165(7):725-30.

Diovan **Diovan HCT**
VALSARTAN VALSARTAN / HYDROCHLOROTHIAZIDE

Angiotensin II AT₁ Receptor Blocker
Please see product monographs for details, available at www.novartis.ca

Member **PAAB** **R&D**

Statins provide, incomparably, more benefit in CHD prevention than diet or exercise.

Clopidogrel: for how long?

4. How long do you treat patients with clopidogrel bisulfate after percutaneous coronary angioplasty and stent, when there is need for warfarin and acetylsalicylic acid (as in severe anterior infarction, left ventricular dysfunction or atrial fibrillation)?


Question submitted by Dr. Mathieu Bernier, Montreal, Quebec

This is a very good question. Unfortunately, there is no good answer, nor is there an answer to be found in any of the large clinical trials. The best that I can do for this question is to give you my opinion.

Clopidogrel is prescribed, as you know, after percutaneous coronary angioplasty (PTCA) and stent, to decrease restenosis due to platelet aggregation. Acetylsalicylic acid (ASA) is prescribed in all coronary artery disease and especially after a MI. Warfarin on the other hand, is prescribed to prevent clot formation as seen in atrial fibrillation or a large apical infarction.

I think it is best to consider each treatment on its own merit. Both ASA and clopidogrel are necessary after PTCA and stent. Warfarin has not been shown to reduce restenosis in this setting.

If warfarin is indicated for other cardiac reasons, I would continue clopidogrel for as long as it is recommended by an interventional cardiologist. In most cases, this should range from one month to six months, but in severe disease, clopidogrel may be prescribed for up to one year. In other words, therapy with warfarin and therapy with clopidogrel should be considered separately.

Only in the case of severe GI disturbances would I eliminate ASA from the regimen as quickly as possible. The next to go would be clopidogrel. In such a setting, it is important to individualize your therapy, choosing the best balance between risk of bleeding and risk of restenosis or clot formation. 

Answered by:

J. Wayne Warnica, FRCPC
 Professor
 University of Calgary
 Director
 Cardiac Intensive Care Unit
 Foothills Medical Centre
 Calgary, Alberta

Therapy with warfarin and therapy with clopidogrel should be considered separately.