


Amiodarone: pearl or peril?

See doi:10.1053/euhj.2001.2986 for the article to which this Editorial refers

In this issue Dr Lumer and co-authors present the economic analysis from the Canadian Trial of Atrial Fibrillation (CTAF)[11]. This trial studied 403 patients with persistent or paroxysmal atrial fibrillation, demonstrating convincing evidence that amiodarone had greater efficacy than sotalol or propafenone in prevention of recurrent atrial fibrillation[2]. The 1 year maintenance of sinus rhythm was 69% in the amiodarone group compared to 39% for sotalol or propafenone. Flowing from this marked difference in efficacy, the authors found lower costs related to atrial fibrillation in the amiodarone group; $532 Canadian dollars in the amiodarone group compared to $898 in the sotalol/propafenone group. This was largely explained by a 40% reduction in cardioversions and a 56% reduction in admissions to hospital with a primary diagnosis of atrial fibrillation in the amiodarone group. It comes as little surprise that a significant reduction in atrial fibrillation results in a significant reduction in resource utilization related to atrial fibrillation care. Unfortunately, the overall cost of care was not significantly different between the two groups because of the nature of the ageing population with significant competing co-morbidities. Atrial fibrillation was responsible for only 28% of the overall cost of care in the study, making the beneficial effect of amiodarone unlikely to impact on overall cost over the time frame of the current study.

The authors are to be commended for providing prospective randomized data that give a concrete clinical and economic basis for use of amiodarone in atrial fibrillation. Other studies in the area have been hampered by relatively small numbers, or cost modelling based on retrospective data collected from multiple small case series or trials that have not provided a ‘head to head’ comparison of amiodarone to other therapies[3,4]. However, even the compelling cost and efficacy data from this trial may not affect most physicians’ decisions to defer the use of amiodarone as a first line drug in most patients with atrial fibrillation. Relatively small cost differences for a short period of follow-up are unlikely to change the culture of antiarrhythmic drug prescription for atrial fibrillation.

Both patients and physicians are wary of ongoing non-cardiac adverse effects related to amiodarone, which can be life-threatening. Open label amiodarone was discontinued in 18% of patients in CTAF, a 64% higher rate of discontinuation than the 11% seen in the sotalol/propafenone group. Although the reason for discontinuation of amiodarone was largely due to reversible or minor side effects, 3% of patients developed pulmonary or neurological findings consistent with toxicity within 1 year of initiation of therapy, which raised concern regarding irreversible organ damage. This rate of amiodarone toxicity and discontinuation is consistent with the results of previous pooled analyses of complications of low dose amiodarone[5,6]. The one exception to clinician avoidance of amiodarone as first line therapy is in patients with poor ventricular function, or those at high risk of proarrhythmia from other antiarrhythmic agents. In these patients, the potential downsides of amiodarone are outweighed by its safety and efficacy.

The second major limitation of the current study is the duration of follow-up. The relatively short 1-year follow-up period in a condition that certainly constitutes a chronic disease raises concern about the long-term confidence in the finding of cost effectiveness. On the one hand, longer follow-up may allow reduced atrial fibrillation in the amiodarone group to result in a reduction in direct costs related to atrial fibrillation, but may also indirectly lead to less progression of underlying heart disease and development of stroke, improving the overall cost benefit of amiodarone. The mortality and stroke impact of maintenance of sinus rhythm is being addressed in the Atrial

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Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial, which may shed indirect light on the merit of use of amiodarone on the grounds of its superior efficacy. On the other hand, a longer duration of follow-up would allow sufficient time for development of amiodarone organ toxicity with its attendant significant costs. The major adverse effects of sotalol and propafenone are predominantly seen early in the treatment course, a time frame that the current study would have captured. The long-term toxicity of amiodarone may result in irreversible organ damage with significant chronic care cost implications. Although surveillance testing for amiodarone toxicity was accounted for in the current analysis, this cost may escalate over time as the cumulative dose increases, accompanied by a progressive increase in lung, thyroid and ocular abnormalities.

Finally, the low cost estimates in this study for certain procedures may actually underestimate the beneficial effect of amiodarone. Thirty Canadian dollars for a Cardiology consultation ($19 US, 22 Euros) or $63 for a cardioversion ($39 US, 44 Euros) represents a significant undervaluation of physician and hospital services in most areas. For example, the US Medicare fee schedule lists $118 US dollars as the charge for a typical clinical consultation. The resultant cost difference between the two treatment strategies in most practice settings is likely significantly higher than the estimate from this trial.

Most clinicians are not surprised by these data, with superior efficacy of amiodarone suggested by other trials and clinical experience showing efficacy in refractory patients. Many will still choose to use propafenone or sotalol as first line agents, not withstanding these data, especially in patients that are not considered at high risk for proarrhythmia, to minimize longstanding exposure to amiodarone. Despite the aforementioned limitations, the authors are to be commended for a strong study that has convincingly demonstrated the superior antiarrhythmic efficacy and short-term cost efficacy of amiodarone in management of atrial fibrillation compared to sotalol and propafenone. Long term follow-up of this patient population may verify the ongoing cost benefit of amiodarone in reducing the cost of atrial fibrillation management, or it may confirm the downside of prolonged exposure to amiodarone.

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References


Intermittent claudication: how should we react to this symptom?

See doi: 10.1053/euhj.2001.3033 for the article to which this Editorial refers

When intermittent claudication is attributed to peripheral arterial disease, the principal issue is whether the patient should be treated specifically to improve walking distance or merely receive optimal therapy for prevention of major cardiovascular events. If specific pharmacological therapy for claudication is utilized, the next issue is...