How European cardiologists perceive the role of calcium antagonists in follow-up after myocardial infarction

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About one hundred European cardiologists discussed the role of calcium antagonists in the follow-up management of myocardial infarction. β-blockers are the treatment of choice. Where these are contra-indicated or otherwise unsuitable, many clinicians would use a non-dihydropyridine calcium antagonist alone or in combination with an ACE inhibitor. There is broad agreement that calcium antagonists should not be used in patients with concomitant left ventricular failure. Cholesterol estimation in post-infarction patients is essential.

Key Words: Calcium antagonists, myocardial infarction, β-blockers, left ventricular failure, ACE inhibitors, cholesterol.

Introduction

Acute myocardial infarction is a spectrum of events ranging from the early phase, soon after the onset of chest pain, through to the late post-infarction phase. There have been few studies of calcium antagonists in the acute phase so there is little evidence that they are of benefit. It is therefore not surprising that only 8% of the participants in the interactive groups were interested in using these agents in the acute early phase of myocardial infarction; 43%, however, would consider using a calcium antagonist after the patient had left the coronary care unit and was in a general ward, or had left hospital and was being followed-up by a physician or cardiologist.

Choice of agent

When it came to the choice of calcium antagonists, the vast majority of participants would use one of the non-dihydropyridines. Only 5% would use a dihydropyridine in a patient who had had a myocardial infarction. Professor Opie suggested that dihydropyridines might be useful on occasion even though no trial data existed to support their use. The only study (SPRINT1-2) had shown no advantage for secondary prevention but the nifedipine used in the study had been the short-acting form which clinicians would not consider using today.

One concern participants expressed about the long-acting dihydropyridines was that the existing data suggest that they fail to reduce the plasma catecholamine level and may even increase it.

Beta-blockade

Ninety percent of the participants thought that beta-blockade should be used in patients who had had a myocardial infarction. European cardiologists have clearly been impressed by the weight of evidence that beta-blockade has a protective effect.

Twenty to 30% of patients have contra-indications to beta-blockers yet, of those who could take the drug, only 50% actually receive it. Clinicians may hesitate to use beta-blockers because patients, particularly elderly ones, complain of tiredness, depression, sleeping problems and reduced capacity for exercise. It is therefore important to look at other methods of secondary prophylaxis. In Denmark, verapamil has become a drug of first choice41.

ACE inhibitors

When beta-blockade was contra-indicated, in patients with respiratory problems or diabetes, for instance,
about 50% of participants would use a non-dihydropyridine calcium antagonist and 31% a combination of a non-dihydropyridine calcium antagonist and an ACE inhibitor.

This was an interesting response because there is no real evidence that ACE inhibitors work as secondary prophylaxis in patients without heart failure though there are some signs that they might. They may have long-term effects by endothelial protection, and perhaps by the production of bradykinin, but they should not be considered as first choice for secondary prevention.

For those who choose a non-dihydropyridine, the evidence of effectiveness is strongest for verapamil though both verapamil and diltiazem are contra-indicated in heart failure.

In deciding between a calcium antagonist alone or in combination with an ACE inhibitor, the actual evidence favours the calcium antagonist but indirect data favour the combination. One attraction of the combination is that the drugs interact with different mechanisms and the clinician may be able to use a lower dose of each drug. In the end the decision is a matter of judgement. There are no hard data defining the 'right' way to manage these patients.

**Secondary prevention**

In the later post-MI stages, when the question of secondary prevention arises, the choice of treatment depends on whether the patient shows evidence of heart failure. For patients who were not in heart failure, the interactive groups agreed that the choice of drug to achieve secondary prophylaxis lay between a beta-blocker and a non-dihydropyridine calcium antagonist. The choice could be based on the expected tolerance and side-effects of a particular drug, or the doctor's familiarity with its use.

**Patients with heart failure**

It was less easy to achieve agreement about the treatment of patients with left ventricular failure though the vast majority of participants agreed that, on present evidence, calcium antagonists should not be used.

Faced with a patient with angina and left ventricular systolic dysfunction (ejection fraction <30%), 31% of participants would use an ACE inhibitor and 45% an ACE inhibitor in combination with beta-blockade. The reasoning behind this choice was that though the ACE inhibitor would have no direct effect on the angina, it could act indirectly. It would allow the left ventricle to maintain an optimal size and shape, reduce oxygen demand and decrease sympathetic release during exercise. It was also suggested that there was reasonable, if not perfect evidence that beta-blockade can be used in these circumstances.

Thirty-five percent of participants thought beta-blockade was contra-indicated because of evidence of deleterious effects on patients with systolic dysfunction and overt heart failure. They pointed out that beta-blockade is still an investigative treatment in these patients. This opinion is shared by the American College of Cardiology which has recently issued a statement that the use of beta-blockade in congestive heart failure is still under evaluation.

The majority of participants felt, however, that there probably was a case for using beta-blockade in the post-infarction stage, though not as sole therapy. They were impressed by the evidence that beta-blockade in carefully given built-up doses may benefit left ventricular failure.

In the discussion, Professor Lüscher pointed out that the patient had a poor prognosis so there was a need not just to treat his symptoms but also to improve his prognosis. ACE inhibitors would do this. For help with his angina, the only option Lüscher would consider was beta-blockade, which might also improve the prognosis. The data in support of beta-blockade were not as solid in patients with an ejection fraction below 30% as they were for those with values above that level. Professor Lüscher would, however, favour treating this patient with a combination of ACE inhibitor and beta-blocker.

Dr Fischer Hansen said there was no real evidence to support the choices the participants had made. In his unit they would use an ACE inhibitor and long-acting nitrates. If that was not effective they might consider using verapamil or a beta-blocker, though he hesitates to give these drugs in patients with poor ventricular function because of the lack of evidence that they offer any benefit to the patient.

**Diabetes and dyslipidaemia**

The case reports included patients who were diabetic, or had a high level of circulating lipids. In those circumstances most of the participants preferred verapamil to a β-blocker, particularly because there is some evidence that verapamil can assist blood glucose control. There is no such evidence for beta-blockers. These drugs may even worsen blood glucose control.

After discussion, all participants agreed that estimation of the blood cholesterol level was an essential investigation in the post-infarction period, and that even in patients with only a moderate degree of lipid elevation, there should be a vigorous attack on cholesterol levels.

This consensus decision reflects the way in which the attitude to cholesterol in secondary prevention has undergone a radical revision. The controversy is clearly over. The evidence now available suggests that in patients with signs of atherosclerosis who have had an infarction, the estimation of cholesterol is mandatory. The level of cholesterol that determines intervention should be set quite low.

Diet and weight control should be used but this group of patients who require not primary but
secondary prevention, need early intervention with drug therapy.

Possible protocols

When classifying patients who have had a myocardial infarction, it is possible to do so in a way that helps determine the type of secondary prevention that should be used. One way of classification (Fig. 1) is to use echocardiography. A left ventricular ejection fraction below 35% is a clear indication for secondary prevention with an ACE inhibitor.

There is less certain information about treatment with β-blockers or with verapamil. The data available suggest that verapamil should be used only in patients with normal or slightly depressed systolic function. β-blockers may be used over a wider range.

Another method of classification is to consider clinical findings during the acute stage of infarction, as was done in the AIRE study and DAVIT II. Patients were then divided into those with and without clinical findings of congestive heart failure (Fig. 2). The AIRE study demonstrated that if patients had had congestive heart failure while in the coronary care unit, they benefited from an ACE inhibitor. DAVIT II showed that verapamil benefited those without heart failure or slightly depressed systolic function.

A third way of classification (Fig. 3) is based on whether the patients had heart failure in the coronary care unit and whether they were still receiving diuretics. Dr Fischer Hansen suggested that a simple, practical approach to the management of patients in the post-infarction stage is to ask: ‘Does this patient need a diuretic?’ If the answer is ‘yes’, he or she should be given an ACE inhibitor. If the answer is ‘no’, secondary prevention should be provided with an anti-ischaemic drug. Dr Fischer Hansen favours verapamil, but a β-blocker could also be used.

All patients need cholesterol control. All of them should also receive aspirin except those who have atrial fibrillation in which case coumarin offers better protection. Low blood flow in a large atrium may encourage fibrin-dependent thrombus formation. Trials in atrial fibrillation suggest that coumarin is superior to aspirin for this particular indication.

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References


Calcium antagonists in myocardial infarction

Case 1

Male, 76 years

Previous history:
- Systemic hypertension for 20 years
- Rare episodes of chest discomfort with exercise
- Episodes of podagra/gout
- Cigarettes 5/day for 60 years

Treatment before admission:
- Metoprolol: 50 mg/day
- Hydrochlorothiazide: 50 mg/day
- Amiloride: 5 mg/day
- Prazosine: 5 mg/day

Status:
- No dyspnoea
- No signs of congestive heart failure
- Blood pressure: 180/120 mmHg
- Heart rate: 48 bpm

Acute treatment:
- APSAC, heparine, aspirin, morphine, oxygen

Uncomplicated cause

What should you know or examine?

Exercise test

<table>
<thead>
<tr>
<th>Load</th>
<th>Heart rate</th>
<th>Systolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>58</td>
<td>150</td>
</tr>
<tr>
<td>50 Watt</td>
<td>96</td>
<td>190</td>
</tr>
<tr>
<td>100 Watt</td>
<td>118</td>
<td>240</td>
</tr>
<tr>
<td>125 Watt</td>
<td>129</td>
<td>240</td>
</tr>
</tbody>
</table>

Rate pressure product:
- Rest: 8700
- Maximal: 30960
- Maximal/Rest = 3.5

Echocardiogram

Left ventricle:
- Diameter in diastole: 44 mm
- Diameter in systole: 33 mm
- Posterior wall thickness: 20 mm
- Septum thickness: 16 mm
- Wall motion index: 1.7 (EF = 50%)
- Left atrial diameter: 48 mm

Which treatment would you administer at discharge?
Regarding AMI, in which phase of AMI do you think calcium antagonists could be used?

Should beta-blockade be used post-MI?

Which drugs are contraindicated in the presence of systolic heart failure and clinical symptoms?

Do you think there are differences between calcium antagonists in relation to post-MI use?

If beta-blockade is contraindicated (respiratory problems, diabetes), which drug(s) would you use?

In post-MI patients with LV systolic dysfunction (i.e. depressed LV ejection fraction <30%) and angina, which of the following drugs is indicated?