How European cardiologists perceive the role of calcium antagonists in the treatment of stable angina

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Some 100 European cardiologists discussed calcium antagonists' role in the management of stable angina. Sixty-two percent of those involved used calcium antagonists rather than beta-blockers as first line therapy; 46% were prepared to use calcium antagonists in patients who had had a myocardial infarction more than 6 months previously. Only one tenth would use calcium antagonists in angina patients with left ventricular dysfunction. There was a broad preference for the use of heart rate-moderating calcium antagonists in most forms of stable angina. The discussions also underlined the diagnostic importance of angiography, exercise testing and lipid profile analysis.

(Eur Heart J 1997; 18 (Suppl A): A113-A116)

Key Words: Calcium antagonists, β-blockers, myocardial infarction, prognosis, diagnosis.

Introduction

The discussion opened with consensus — a unanimous acceptance of the first new definition of angina for 200 years: 'Angina pectoris is a symptom complex in which discomfort in the chest and adjacent areas is attributable to myocardial ischaemia. It is most commonly due to coronary atherosclerosis but may be secondary to such disorders as aortic stenosis and hypertrophic cardiomyopathy.' Consensus on appropriate treatment proved less easy to achieve.

First line therapy

When treating patients with stable angina, 62% of participants were using calcium antagonists rather than beta-blockers as first line therapy. 46% would use calcium antagonists in patients who had had a myocardial infarction more than 6 months before, but only 10% would use them in patients with angina who had left ventricular dysfunction.

Which agent?

When participants were asked which calcium antagonist they would use in patients with chronic effort angina, few (13%) said they would choose dihydropyridines. Most would use heart rate-moderating calcium antagonists — 48% would use verapamil, 39% diltiazem. This was an unexpected response and does not reflect the current sales, and presumably usage of these agents.

Coronary vasospasm

When asked what they would use in angina caused by spasm — which seems to be reported more often in Japan and Italy than in other countries — most participants (58%) chose dihydropyridines. This again was an interesting reflection of current attitudes because nearly all of Maseri's early data on the effectiveness of calcium antagonists in coronary spasm had come from the use of verapamil.

It was clear that the participants believed that the effect on heart rate was important in chronic stable angina but in vasospasm they preferred the dihydropyridines for their effect on smooth muscle.

Ventricular dysfunction

When asked which calcium antagonist is most suitable in patients with left ventricular dysfunction about 45% of participants chose dihydropyridines. 38% would use verapamil and 17% diltiazem.

Prognosis

Although no recent study has shown that any drug other than aspirin can improve the prognosis in angina pectoris, 49% of participants felt that the heart rate-moderating calcium antagonists also had a proven
Calcium antagonists vs beta-blockers

Discussion of the relative advantages of calcium antagonism and beta-blockade had largely been pre-empted by the publication just before the meeting of the two largest studies ever made of stable angina.

TIBET — the Total Ischaemic Burden European Trial — had investigated the effects of atenolol, nifedipine and their combination on exercise parameters and ambulatory ischaemic activity in 608 patients with chronic stable angina. Both drugs, alone and in combination, produced the same outcome — a significant improvement in exercise parameters and a significant reduction in ischaemic events during normal everyday activities.

APSIS — the Angina Prognosis Study in Stockholm — was a more powerful study than TIBET. It had compared the long-term treatment effects of metoprolol and verapamil in 809 patients with stable angina pectoris. Both drugs had been well tolerated and there had been no difference between them in their effects on mortality, cardiovascular end-points, and measures of quality of life (Table 1). The annual mortality and cardiovascular event rates in APSIS had been 1.7% and 8.4%, respectively. The follow-up period in TIBET had been 2 years. The median follow-up time in APSIS had been 3-4 years (2766 patient years).

The class of agent that participants chose as first line therapy in stable angina seemed to be determined by their familiarity with a particular drug, their experience of its effectiveness and of how well it was tolerated, and their overall 'clinical impression'.

The need for hard data — and the demographic variation in 'clinical impression' — emerged during the setting-up of TIBET. The investigators had some difficulty persuading clinicians to participate. The reasons for reluctance were different in Northern and Southern Europe. In Northern Europe clinicians thought it dangerous to use nifedipine in patients with angina pectoris; in the South they considered it dangerous to use atenolol in these patients. In the end, the outcome with both drugs was the same.

The APSIS investigators avoided the acceptance problem by choosing verapamil as the calcium antagonist because they wanted one that did not increase the heart rate. They also wanted one that they could use at comparatively high dosage.

Angiography

Discussion of the case histories revealed demographic differences in the clinical approach to coronary angiography. In some places, particularly in Scandinavia, angiography was seen as a step towards revascularization. In other places it was more often used as a diagnostic process — to evaluate patients rather than as a first step in their treatment.

Those who argued against the technique being used purely as a diagnostic process suggested that, before clinicians sent a patient for angiography, they should have decided what sort of management they intended to deploy when they saw the result. Otherwise, they might be tempted to use percutaneous transluminal coronary angioplasty when any lesion was found, even one that was located distally, was only in one vessel, and was causing the patient no severe symptoms.

Those in favour of using angiography diagnostically argued that there was no certain way of identifying the high risk patient with non-invasive tests. After discussion, a consensus emerged that angiography could perhaps be used more frequently.

More frequent use of angiography would have particular implications for women. Many women with severe symptoms turn out to have normal coronary arteries. Those in whom this could be established would be spared having to take unnecessary drugs. The discussion included a reminder that coronary heart disease begins ten years later in women than in men. A 60-year-old woman therefore needs to be considered in the same way as a 50-year-old man.

Exercise testing

Participants also agreed, after discussion, that all patients with stable angina should have exercise tests, though not necessarily for diagnosis. They could be used as a non-invasive, if not absolutely certain, way of detecting patients at high risk. A patient in whom exercise testing was positive at a low workload, the clinician would consider performing angiography much earlier than in one who could tolerate higher workloads.

Lipids

We were surprised that some participants did not include a lipid profile as one of their routine investigations.
in patients with stable angina. Evidence now available suggests that the estimation of cholesterol should be a mandatory investigation in patients with angina, and that the level of cholesterol that determines intervention should be set quite low. When the strength of the evidence was discussed, all participants accepted the need for mandatory testing.

Aspirin

Participants agreed that all patients with stable angina should receive aspirin because of the evidence that it improves the prognosis in these patients.

The authors would like to acknowledge the assistance of Dr Michael O'Donnell and Paul Castle in the preparation of the manuscript.

References

In which circumstances should calcium antagonists be considered in the therapy of stable angina?

- 62%: First line therapy
- 46%: Patients with previous myocardial infarction
- 10%: Patients with left ventricular dysfunction

Which is the most suitable calcium antagonist in patients with chronic effort angina?

- 13%: Dihydropyridines
- 39%: Diltiazem
- 48%: Verapamil

Which is the most suitable calcium antagonist in patients with coronary vasospasm?

- 58%: Dihydropyridines
- 24%: Diltiazem
- 18%: Verapamil

Which is the most suitable calcium antagonist in patients with known left ventricular dysfunction?

- 45%: Dihydropyridines
- 17%: Diltiazem
- 38%: Verapamil

Which calcium antagonists have been shown to improve prognosis in patients with stable angina?

- 49%: Dihydropyridines
- 45%: Heart-rate moderators
- 9%: None

Eur Heart J, Vol. 18, Suppl A 1997