Verapamil
A Review of its Pharmacological Properties and Therapeutic Use in Coronary Artery Disease

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Verapamil has well proven efficacy in the treatment of patients with hypertension, and early studies indicated its efficacy in the treatment of coronary artery disease. The efficacy of verapamil relative to placebo in patients with stable angina pectoris is confirmed, and the drug is at least as effective as nifedipine, propranolol or metoprolol and of similar efficacy to bepridil and nicardipine when administered as a conventional or sustained release formulation.

Verapamil is the first calcium antagonist to be shown in a double-blind study to significantly reduce mortality and reinfarction rate after acute myocardial infarction in patients without heart failure. In these patients, the reduction in mortality achieved with verapamil was similar to that reported with β-adrenoceptor antagonists, suggesting that verapamil may be a suitable alternative to β-blockers as secondary prevention in patients intolerant of these drugs.

Recurrence of stenosis in patients who successfully undergo percutaneous transluminal coronary angioplasty (PTCA) limits the usefulness of the procedure. Verapamil has recently been shown to significantly reduce the rate of restenosis in patients with stable angina at risk of recurrence, although these initial results require confirmation.

Verapamil, therefore, is effective in the treatment of patients with stable angina pectoris, appears to be an alternative to β-blockers in selected patients as late start secondary prevention after acute myocardial infarction and has a potential role in preventing recurrent stenosis after PTCA, if initial results are confirmed.

Single intravenous doses of verapamil lower blood pressure, increase heart rate, decrease systemic vascular resistance and increase cardiac output in patients with coronary artery disease. However, during 4 weeks' treatment with verapamil 360mg daily blood pressure is decreased by only about 10% in patients without hypertension, and cardiac output, resting and exercise heart rate are unaffected. Assessment of the effects of oral verapamil on left ventricular function using doppler echocardiographic techniques revealed changes indicative of improved early filling and enhanced relaxation, although studies employing both invasive and noninvasive techniques reported a variable effect of intravenous verapamil on diastolic function. Generally however, the negative inotropic effect of verapamil is counterbalanced by its vasodilatory effect and consequent reduction in afterload. When administered intravenously, verapamil decreased coronary vascular resistance without altering myocardial oxygen consumption, or vice versa, in patients with coronary disease. The effect of verapamil on double product has also varied, with results ranging from significant to non-significant reductions.

Experimental studies have shown that calcium overload of the arterial wall is important to the pathogenesis of atherosclerotic lesions. Additionally, by inhibi-