Probable adverse interaction between oral metoprolol and verapamil

J. N. H. EISENBERG
M.R.C.P.

G. D. G. OAKLEY
M.R.C.P.

Department of Medicine and Cardiothoracic Unit, Northern General Hospital, Herries Road, Sheffield S5 7AU

Summary
A combination of an oral beta-adrenergic blocking agent and verapamil has been advocated as a safe treatment for angina. A case of Wenckebach type atrioventricular block occurring in a patient on metoprolol and verapamil is reported. It is suggested that this combination is used with caution.

KEY WORDS: atrioventricular heart block, angina.

Introduction
It is well documented that the use of intravenous verapamil in patients on beta-adrenergic blocking agents can cause adverse circulatory effects (Krikler, 1974). Recent work has, however, advocated the combined use of oral verapamil and beta-blockers as a safe and effective treatment for angina (Subramanian et al., 1982; Packer et al., 1982).

We report a case of rest angina of increasing severity in which this oral combination produced a potentially serious bradycardia.

Case report
A 46-year-old male with no significant past history was admitted with angina at rest of increasing severity over a period of 3 weeks. This was not associated with any electrocardiographic (ECG) or enzyme evidence of established myocardial infarction.

He had been initially treated with metoprolol 50 mg twice daily, verapamil 80 mg three times daily and glyceryl trinitrate as required. His resting pulse rate on this regimen was 80/min. The angina worsened despite treatment. The metoprolol dosage was increased to 100 mg twice daily and the verapamil was continued unchanged.

Two hours after his second dose of metoprolol, 100 mg, he developed transient episodes of bradycardia 44/min, during which he felt faint and unwell. ECG showed his rhythm to be Wenckebach type atrioventricular (AV) block interspersed with sinus rhythm (Fig. 1). Verapamil was discontinued, metoprolol maintained at 100 mg twice daily and nifedipine, 10 mg three times daily, added. Within 6 hr of stopping the verapamil his episodes of bradycardia ceased.

Despite further increases in therapy his angina persisted, so coronary angiography was performed. This showed an isolated stenosis of the left anterior descending artery, but no lesion in the right circumflex artery. The left anterior descending artery lesion was treated successfully by angioplasty.

Comment
The dangers of intravenous verapamil in patients on beta-blockers are well known. The treatment of angina with combined oral verapamil and beta-blockers is becoming frequently used. Problems of conduction disturbances have been reported only rarely (Subramanian et al., 1982; Packer et al., 1982). This patient developed symptomatic bradycardia
associated with Wenckebach type AV block on oral verapamil and metoprolol.

It is possible that verapamil alone may have had this effect but previous work suggests this is unusual, particularly at low oral doses (Leon et al., 1981). Studies of the combination of verapamil and beta-blockers have mainly used propranolol. It is feasible, though unlikely, that metoprolol has a different effect from propranolol in this situation.

Prolongation of the PR interval with verapamil therapy is a common occurrence and therefore does not act as an early warning sign of greater degrees of block (Leon et al., 1981).

However a previous report (Wayne et al., 1982) cites two cases of bradycardia (one sinus, one junctional) occurring on oral metoprolol and verapamil, in which atropine in a dose of up to 1·8 mg did not significantly increase heart rate. AV conduction promptly improved upon discontinuing verapamil in the present case so atropine was not used.

It is always possible that impaired conduction is due to ischaemia. Wenckebach type AV block is, however, usually associated with disease of the right coronary artery but in our case this was subsequently shown to be normal and dominant. This suggests that the conduction disturbance was entirely due to drugs.

The importance of effective treatment in angina at rest means that the risk of possible side effects is less a contraindication than in chronic stable angina. In view of the potential problems it would therefore seem reasonable to use this combination with caution, to have facilities for intensive monitoring available and be ready to withdraw verapamil at the earliest sign of serious bradycardia.

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References


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J. N. Eisenberg and G. D. Oakley

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