PERIPHERAL HAEMODYNAMIC EFFECTS OF PINDOLOL

O. OHLSSON

Central Hospital, S 291 85 Kristianstad, Sweden

Although during the last 10 years the β -adrenoceptor blockers have proved themselves to be effective and well tolerated drugs for the treatment of essential hypertension it is recognized that their use is occasionally associated with the occurrence of specific side effects. These side effects include peripheral circulatory disturbances which are often manifested as cold hands and feet. The prevalence of this effect varies widely between different studies and rates between 5% (Dafgard, 1978) and 30% (Marshall *et al.*, 1976; Wilcox, 1980; Zacharias, 1976) have been reported. In an unselected series of hypertensive patients aged under 60 years, we found that 10% complained of cold extremities during treatment with β -adrenoceptor blockers. However, in our experience this side effect is less common in patients treated with pindolol, a β -adrenoceptor antagonist which exerts relatively pronounced sympathomimetic effects (Mattiasson, 1979).

The present study, which has been reported in full elsewhere (Ohlsson & Lindell, 1981), was carried out to investigate whether a change in therapy would result in an increase in hand blood flow in patients complaining of cold extremities during treatment with β -adrenoceptor antagonists.

The study was carried out in a group of nine hypertensive patients (eight men and one woman) who had been treated with a β -adrenoceptor blocker (atenolol in eight cases, propranolol in one) alone or in combination with a diuretic for at least 6 months, all of whom complained of cold extremities. While the patients were still receiving the β -adrenoceptor blocker inducing cold extremities hand blood flow was measured in both hands by venous occlusion plethysmography (Dahn, 1965) and peripheral vascular resistance was calculated by dividing mean arterial pressure by hand blood flow. The patients were then randomly assigned to one of two groups which received either the original medication plus prazosin (2×0.5 mg daily) or pindolol (10 mg once daily) alone.

This treatment was continued for 2 weeks during which hand blood flow was again measured. Following this the patients treated with pindolol were transferred to the original β -adrenoceptor blocker plus prazosin and *vice versa* for a further 2 weeks and hand blood flow again measured. In those patients who

had previously received additional diuretic therapy this was continued throughout the investigation. During each treatment period the patients were evaluated for subjective symptomatic changes.

It was found that addition of prazosin to the original medication did not produce any statistically significant changes in blood pressure, heart rate, hand blood flow or vascular resistance. One patient who showed a small increase in hand blood flow reported a subjective improvement in symptoms.

When the original β -adrenoceptor blocker was replaced by pindolol, blood pressure remained unchanged but heart rate increased significantly by 6 beats/min ($P < 0.01$). In addition hand blood flow was increased from 11.7 to 15 units ($d = 3.34 \pm 2.67$, $P < 0.01$) and this was associated with a fall in resistance from 9.5 to 7.2 units ($d = 2.2 \pm 2.0$, $P < 0.05$). These haemodynamic changes were accompanied by a disappearance of sensitivity to cold in five patients after changing to pindolol. A further three patients reported a subjective improvement in symptoms and one patient who did not show an increase in hand blood flow after changing to pindolol reported no change in symptoms.

The mechanism whereby β -adrenoceptor blockers induce cold extremities is not completely understood. It has been suggested that blockade of vascular β_2 -adrenoceptors may result in vasoconstriction due to unopposed α -adrenoceptor stimulation. However, the fact that β_1 -selective antagonists produce this side-effect with about the same frequency as non-selective drugs suggests that the vasoconstriction is reflex in origin and is provoked by a reduction in cardiac output. In a recent study the effects of β -adrenoceptor blockers with and without ISA on heart rate blood pressure and cardiac output at rest were measured in healthy volunteers and it was concluded that drugs with ISA may produce less depression of cardiac output than antagonists lacking this property (Lysbo Svendsen *et al.*, 1979). Thus, at equipotent doses, atenolol and propranolol decreased resting cardiac output by 27 and 21% respectively while pindolol was without effect on this parameter.

Surprisingly we found no increase in hand blood flow or subjective improvement following the addition of prazosin in the original medication despite the fact that this drug is reported to be a potent vas-

odilator (Collier *et al.*, 1978). A possible explanation of this finding may be the short duration of action of prazosin.

It may be concluded from the results that a β -

adrenoceptor blocker with pronounced ISA such as pindolol appears to be the drug of choice in patients suffering from cold extremities during β -adrenoceptor blocker therapy.

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