INTRAVENOUS LABETALOL IN SEVERE HYPERTENSION

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1 Labetalol was administered by intravenous infusion or by the combination of intravenous bolus injection plus infusion to 15 patients with severe essential hypertension and to one with phaeochromocytoma.

2 With the infusion alone the reduction of arterial pressure was slow to develop and limited in degree, but with the combination of the bolus injection plus the infusion the reduction in pressure was more prompt, more pronounced and longer lasting. Apart from an uncomplicated syncopal attack in one patient, no serious side — effects were encountered.

3 Subsequent treatment with oral labetalol usually required the addition of a diuretic to control the blood pressure probably due to sodium and fluid retention during treatment with labetalol alone.

Introduction

Labetalol, the combined α - and β -adrenoceptor-blocking agent, has been shown to be very effective in the treatment of hypertensive crises when given intravenously (Agabiti-Rosei *et al.*, 1976; Cumming *et al.*, 1979). Compared with other anti-hypertensive drugs used in these situations, it has the advantage that treatment can be continued with the oral preparation.

In this study we assessed the value of labetalol in the treatment of hypertensive crises when given by bolus injection and/or infusion, and the short-term effect of continual oral treatment.

Methods

Fifteen patients with severe essential hypertension together with a single patient known to have a phaeochromocytoma were treated with labetalol intravenously. Initial mean blood pressure for the entire group was 240/155 mmHg ($\pm 10/6$ s.e. mean). Fourteen patients, including the patient with phaeochromocytoma, received a bolus injection of labetalol 100 mg over 2 min, followed, except in one case, by an intravenous infusion at the rate of 2–4 mg/min for 60–90 min. A total of 17 hypertensive crises were treated in this way. Two other patients received intravenous infusions: one at the rate of 0.5 mg/min and the other of 2 mg/min, lasting 3 h.

One hour after the end of each infusion, oral labetalol 200 mg three times daily was started. Diuretics (hydrochlorothiazide 50 mg combined with amiloride 5 mg daily) were added when blood pressure remained inadequately controlled by labetalol alone (diastolic blood pressure >110 mmHg).

Results

Intravenous treatment

In 11 of the 12 patients with essential hypertension treated with a combination of bolus injection plus infusion a 30% fall in both systolic and diastolic blood pressures was achieved within 5 min (Figure 1). Thereafter blood pressure remained effectively controlled throughout the infusion period and during the first 24 h of oral labetalol administration. In one patient blood pressure was not adequately controlled despite an infusion rate of 4 mg/min. In another patient with essential hypertension there was an immediate and profound reduction in blood pressure following a single bolus injection and in this patient an infusion was not given. Except for transient orthostatic hypotension during the period immediately following the infusion no other serious side-effects were encountered.

In the two patients treated with the infusion of labetalol without bolus the reduction in blood pressure occurred slowly and was limited in degree even at the high dose of 2 mg/min. The mean reduction in systolic blood pressure was approximately 30% and in diastolic blood pressure approximately 20%. These pressures were achieved 1 h after starting the infusion (Figure 2).

The patient with phaeochromocytoma was treated on four occasions with the bolus injection plus infusion and each time a prompt and marked fall in blood pressure occurred without side-effects.

Oral treatment

Thirteen patients, two treated with the infusion alone and 11 treated with the bolus plus infusion,

Figure 1 Blood pressure response to a combination of bolus injection and infusion of labetalol followed by oral administration for 24 h. $n = 11$ (nine male, two female).

Figure 2 Blood pressure response to intravenously infused labetalol in two male patients with hypertensive crises. BP, Blood pressure; HR, heart rate.

continued on the oral preparation. Five were still well controlled after 2 weeks. In the other eight, however, progressive increases in blood pressure required the addition of diuretics. After 4 weeks three patients were still well controlled with oral labetalol alone, whereas the other ten were well controlled with labetalol plus diuretic.

Discussion

In 12 of the 13 patients in whom a combination of bolus injection and infusion were used, the fall in blood pressure was more prompt, more pronounced and longer lasting than in the two patients treated with infusion alone, and no serious side-effects occurred. It has rightly been emphasized that when blood pressure is lowered too precipitately in hypertensive crises there is a risk of causing cerebral infarction (Strangaard *et al.*, 1973; Graham, 1975; Mackay *et al.*, 1981).

Myocardial ischaemia may also occur with the use of hypertensive agents which cause tachycardia and increase in cardiac output (Brown *et al.*, 1977). In our patients the prompt and marked fall in blood pressure was not accompanied by severe side-effects except in one case of syncope but without signs of focal neurological lesion. In our experience the combination of bolus injection plus the infusion of

labetalol was superior to the infusion alone in the treatment of hypertensive crises and we found it to be safe in use. It also seems preferable to the bolus injection alone, as the percentage of responders in our series is much higher than that found by some authors who used the bolus injection without infusion (McGrath *et al.*, 1978; MacCarthy *et al.*, 1978). It is clear that when labetalol is infused intravenously after a bolus injection, the plasma concentration of labetalol remains higher for a longer time, causing a more marked and prolonged depressor effect. We conclude therefore that the combination of bolus injection plus the infusion of labetalol is efficacious and safe in the treatment of hypertensive crises.

In the same patients with severe hypertension successfully treated with the bolus injection plus infusion, long-term treatment with oral labetalol alone was not as satisfactory. It was necessary to add a diuretic to the treatment regime of the majority in order to maintain control of blood pressure. It has been shown previously that a progressive expansion in extracellular fluid volume can occur in some patients treated with oral labetalol (Weidmann *et al.*, 1978). In our patients, blood pressure became well controlled after a diuretic was added, thus lending support to the view that expansion of circulating volume did occur in most of our patients during treatment with labetalol alone.

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