BLOOD PRESSURE OVER-SHOOT DUE TO ACUTE CLONIDINE (CATAPRES) WITHDRAWAL: STUDIES ON ARTERIAL AND URINARY CATECHOLAMINES AND SUGGESTIONS FOR MANAGEMENT OF THE CRISIS

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SUMMARY

1. Clonidine was withdrawn acutely in five hypertensive patients with a documented blood pressure over-shoot after previous temporary cessation of treatment.

2. In all patients a severe rise of systolic and diastolic blood pressure was seen (average 67/58 mmHg). This was accompanied by a number of 'withdrawal symptoms', e.g. restlessness, tremor, headaches and nausea.

3. Catecholamines in urine rose from 32 pg/l to 112 pg/l (0.01 < P < 0.02) and in arterial blood from 0.52 µg/l to 1.0 µg/l (not significant).

4. The crisis could be reversed acutely by α- and β-adrenergic blockade.

5. Catecholamine depletion with reserpine before the withdrawal of clonidine seemed to reduce the blood pressure rise and the withdrawal symptoms.

Key words: withdrawal of clonidine, blood pressure over-shoot, α- and β-adrenergic blockade, reserpine pretreatment, catecholamines.

Clonidine is an imidazoline derivative with blood pressure-lowering properties (Hoobler & Sagastume, 1971). Both central nervous effects (Shaw, Hunyor & Korner, 1971a) and peripheral vascular effects have been demonstrated (Shaw, Hunyor & Korner, 1971b). Withdrawal of clonidine may cause a rebound phenomenon, which has been pointed out by Hökfelt, Hedeland & Dymling (1970).

The purpose of the present investigation was to study the effects of acute withdrawal of clonidine particularly with regard to changes of blood pressure and arterial and urinary catecholamines.

MATERIALS AND METHODS

Five patients with moderate to severe essential hypertension were included in the study. All

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were treated with clonidine for 2–4 years. Their daily dosage of clonidine was 0.3–2.4 mg. These patients were selected because of a documented blood pressure over-shoot during a previous temporary withdrawal of clonidine. After informed consent was obtained, the patients were hospitalized for baseline studies including arterial and urinary catecholamines. The fluorimetric technique of von Euler & Lishajko (1961) was used in the estimation of catecholamine levels.

At 10 p.m. on the third day placebo was substituted for clonidine. It was predetermined to use α- and β-adrenergic blockers should a blood pressure crisis occur.

Finally, having gained the experience of patients 1–4, it was decided to try to alter the course by means of catecholamine depletion. Thus patient 5 was pretreated with reserpine (1 mg intramuscularly twice daily for 3 days) before the withdrawal of clonidine.

RESULTS

All patients noted the change of treatment within a few hours. Initially they complained of insomnia and restlessness; later headaches, tremor, nausea, stomach pains and muscle pains were reported.

Blood pressure rose in all patients, most markedly in patients 1–4. The average rise in all patients was from 149/103 mmHg (average of four recordings during the preceding day) to 216/161 mmHg (recorded at approx. 12 h after withdrawal). Both the systolic (67 mmHg) and the diastolic (58 mmHg) rises were statistically significant (0.005 < P < 0.01). Average heart rate increased from 73 to 85 beats/min (NS).

In patients 1, 2 and 4 intravenous administration of propranolol (0.2 mg/kg) gave an almost immediate relief from most of the symptoms, but had no effect on the blood pressure. However, after additional phentolamine (i.v., 20–30 mg), there was a drop of blood pressure to an average of 169/117 mmHg (0.001 < P < 0.01 systolic, 0.01 < P < 0.02 diastolic).

In patient 3 it was possible to reduce the blood pressure gradually from a peak of 200/135 mmHg towards the initial level of 120/80 mmHg over a 48 h period by means of oral propranolol (40 mg) four times daily and dibenzyline (20 mg) four times daily.

Patient 5 who was pretreated with reserpine had a markedly milder course. Although he developed the same withdrawal symptoms as the other patients, these were of a much milder degree. The rise of blood pressure was also less pronounced (from 130/95 to 175/120 mmHg) and acute treatment with propranolol and phentolamine was not given. The average urinary catecholamine levels in patients 1–4 rose from 32 to 112 µg/24 h (0.01 < P < 0.02), whereas arterial catecholamines rose from 0.52 to 1.0 µg/l (NS). Again the changes were less in patient 5; urinary catecholamines rose from 14.7 to 44.9 µg/24 h and arterial catecholamines from 0.74 to 0.89 µg/l.

DISCUSSION

Acute withdrawal of clonidine in five patients who all had been on chronic treatment caused a rather alarming rise of blood pressure. This was accompanied by an array of symptoms, e.g. insomnia, restlessness, tremor and headaches. Urinary and arterial catecholamines rose markedly. This finding in combination with the response to α- and β-adrenergic blockers indicates that the blood pressure crisis may result from an increased sympathetic discharge.
Clonidine withdrawal

As all our patients were selected because of a previous over-shoot it is not possible to draw conclusions regarding the frequency with which this rebound phenomenon can be expected. Obviously it is reproducible. Regarding the management of the crisis the most logical step of course is reinstitution of clonidine. However, our data suggest that \( \alpha \) - and \( \beta \)-adrenergic blockers may be useful in this respect. Finally, it seems possible to alter the course by pretreatment with reserpine before withdrawal of clonidine.

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REFERENCES


