ACCELERATED ACUTE CLONIDINE WITHDRAWAL SYNDROME DURING CORONARY ARTERY BYPASS SURGERY

A case report

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SUMMARY

A patient with essential hypertension treated with clonidine developed accelerated acute clonidine withdrawal syndrome during coronary artery bypass surgery. There were recurring hypotensive and hypertensive episodes. The hypotension was associated with myocardial ischaemia, cardiac arrhythmia and ventricular fibrillation, and was treated successfully with i.v. calcium chloride given at the onset of hypotension.

Clonidine (Catapres) is an imidazoline derivative closely related chemically to tolazoline. It is an antihypertensive agent which acts centrally to reduce sympathetic nervous system activity and peripherally to produce alpha blockade by acting as a partial agonist. It increases vagal tone and the sensitivity to baroreceptor reflexes (Goodman and Gilman, 1975). Chronic administration reduces plasma renin activity (Kosman, 1975).

A patient receiving clonidine developed exceptional hypotensive and hypertensive changes during and following coronary artery surgery.

CASE REPORT

A 52-yr-old man was admitted to hospital for coronary artery surgery. He had a history of essential hypertension which had been treated with oral clonidine 0.15–0.2 mg per day for 6 yr. Seven months before surgery he developed angina and 2 weeks later suffered an inferior myocardial infarction. Following this, he was asymptomatic for 4 months until he began having recurrent episodes of angina pectoris. Coronary angiography was performed and showed inferior akesia and triple vessel disease. He was treated with propanolol and isosorbide without improvement of the angina and vein grafting was proposed.

The patient was plethoric (body weight 77 kg). The heart was in sinus rhythm, and the arterial pressure was 130/80 mm Hg. E.c.g. showed an old inferior infarction but no left ventricular hypertrophy. Other relevant tests gave normal results. Current treatment was clonidine 0.1 mg twice daily, propranolol 40 mg thrice daily and bendrofluazide 5 mg with potassium. The last dose of these drugs was given on the night before operation.

On the morning of surgery the patient was premedicated with diazepam 20 mg orally 2 h before operation, followed by papaveretum 20 mg and hyoscine 0.4 mg i.m. 1 h before operation. Anaesthesia was induced with papaveretum 20 mg, thiopentone 175 mg and pancuronium 12 mg administered i.v. The systolic arterial pressure was 155 mm Hg on arrival in the operating room, and decreased by about 15 mm Hg following induction. The trachea was intubated and the lungs ventilated artificially to keep $P_{\text{a,CO}_2}$ within the normal range. Cannulae were inserted to the left brachial artery, right internal jugular vein and a peripheral vein in the right arm. Anaesthesia was maintained with nitrous oxide; intermittent doses of pancuronium, papaveretum and diazepam were given i.v.

The arterial pressure increased steadily during opening of the thorax despite the administration of papaveretum 40 mg, diazepam 15 mg and halothane 1.5%. When the systolic pressure reached 200 mm Hg, phentolamine 3 mg was administered and the pressure decreased to 140 mm Hg. During cardiopulmonary bypass the perfusion pressure was high, between 110 and 120 mm Hg and a total of 13 mg of phentolamine was given, each increment reducing the pressure to 90 mm Hg.

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On cessation of cardiopulmonary bypass the systolic arterial pressure was 100 mm Hg. During the next hour the pressure ranged from 120 to 150 mm Hg. Closure of the chest was uneventful, but soon afterwards the arterial pressure started to decrease. At about 115 mm Hg systolic the e.c.g. showed marked ST segment depression and ventricular extrasystoles. As the arterial pressure decreased further ventricular fibrillation occurred, despite a normal serum potassium concentration (4.4 mmol litre⁻¹). The heart was successfully defibrillated, but because the arterial pressure remained low, an isoprenaline infusion was commenced. Within minutes the arterial pressure increased to 240 mm Hg and tachycardia developed. The ST segment returned to normal with the increase in arterial pressure. On discontinuing isoprenaline, the arterial pressure again decreased with e.c.g. signs of myocardial ischaemia, until, at a pressure of 90 mm Hg systolic, the heart fibrillated again. On this occasion dobutamine 1 mg kg⁻¹ min⁻¹ was administered as a continuous infusion, but within about 5 min the arterial pressure increased to 240 mm Hg, decreasing after dobutamine was discontinued. Subsequently, as the arterial pressure decreased, calcium chloride 2–3 mmol was administered i.v. and effectively prevented marked hypotension and e.c.g. changes. Three further episodes of hypertension followed by hypotension occurred before the patient was transferred to the intensive therapy unit, calcium chloride being used to modify each hypotensive phase.

Ventricular fibrillation occurred shortly after arrival in the intensive therapy unit. This time it was attributed to the serum potassium concentration, which had decreased to 3.5 mmol litre⁻¹. Despite successful defibrillation and administration of potassium, ventricular extrasystoles persisted and an i.v. infusion of lignocaine was commenced at a rate of 1 mg min⁻¹. A total of 240 mmol of potassium chloride was subsequently required in the first 24 h to maintain the serum potassium between 4.6 and 5.2 mmol litre⁻¹, the range in which there were no ventricular ectopic beats.

Hypertensive surges of decreasing severity continued for 4 h and hypotension was treated during the 1st hour with calcium chloride. Six hours after operation the “baseline” arterial pressure decreased to 100 mm Hg systolic and ST depression recurred on the e.c.g. A dopamine infusion was therefore started at a rate of 1 μg kg⁻¹ min⁻¹ and used to maintain the arterial pressure greater than 120 mm Hg systolic. On this occasion no excessive sensitivity to the inotrope was observed. The lungs were ventilated overnight and the patient sedated with either diamorphine 1–2 mg or diazepam 2.5 mg administered i.v. as necessary. After 12 h the dopamine infusion was discontinued.

For the next 48 h the systolic arterial pressure ranged from 130 to 150 mm Hg, but on the 3rd day the pressure became consistently more than 150 mm Hg and hydralazine 25 mg thrice daily was commenced by mouth. This treatment was effective. The rest of the course after operation was uneventful. At no time was any neurological deficit detected. The patient was discharged on the 14th day after the operation.

**DISCUSSION**

This patient showed unusual resistance to measures commonly effective in reducing arterial pressure under anaesthesia, and in the post-bypass phase there were dramatic cyclic changes in arterial pressure. The pattern of these cycles was reminiscent of a servo system hunting for the mean. The hypertensive phases were well tolerated, whereas the hypotensive phases precipitated myocardial ischaemia, arrhythmia and ventricular fibrillation. Changes in arterial pressure occur commonly during and after coronary artery surgery, but regular cycles of hypotension followed by hypertension are most unusual. While inadequacy of a graft may have been responsible for the ischaemia which occurred with hypotension, it does not cause cyclic arterial pressure changes. It seems likely that these changes were precipitated as a result of clonidine withdrawal.

Acute clonidine withdrawal syndrome is well documented (Kosman, 1975; Reid et al., 1977; Geyskes, Boer and Dorhout Mees, 1979). Onset of the syndrome, characterized by hypertension, tachycardia, agitation and vomiting, can occur as early as 8 h after cessation of therapy (Hunyor et al., 1973), but is more usually seen some 18–24 h afterwards and the condition may persist for 2 weeks if untreated. Hypertensive encephalopathy may occur and several deaths have been reported (Bulletin, 1977). Withdrawal is more likely if the patient has been on high doses of clonidine in the range of 0.9–2 mg per day (Reid et al., 1977). Little information is available concerning clonidine withdrawal and anaesthesia (Brenner and Lieber-
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The first two of these reports are of patients undergoing cardiopulmonary bypass. Sustained hypertension occurred in one patient and in the second, cyclic changes in arterial pressure developed. However, few details of the latter case were published, although swings in arterial pressure from 240 mm Hg to 60 mm Hg were observed (Spotnitz, 1978).

In this patient the administration of catecholamines was associated with excessive hypertension. Increased sensitivity to administered catecholamines has been reported in patients exhibiting clonidine withdrawal (Hökfelt, 1974). In contrast, the use of small doses of calcium chloride 1–4 mmol i.v. in this patient modified the hypertensive phases and prevented ventricular fibrillation.

Ventricular fibrillation occurred on three occasions and it was only when the serum potassium concentration was relatively high after operation that the patient was free from ventricular ectopic beats. Although ventricular fibrillation was attributed to hypotension, clonidine withdrawal may have reduced the threshold to fibrillation. There is some evidence of such an effect in animals (Rotenberg et al., 1978).

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REFERENCES

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