SIDE EFFECTS OF DRUGS

Hypotension during angiotensin blockade with saralasin

Angiotensin blockade with saralasin (1-sar-8-ala-angiotensin II) has been suggested as a valuable procedure to detect the angiotensin dependence of several forms of hypertension.¹ Saralasin is usually administered after sodium depletion because pre-existing hypervolaemia may blunt the blood pressure's response to the drug. Hypotensive reactions induced by saralasin have not been reported except in patients simultaneously receiving other antihypertensive drugs, particularly vasodilating agents such as minoxidil or hydralazine.² We report a case of severe hypotension during saralasin infusion in a patient suffering from renovascular hypertension and not receiving vasodilating antihypertensive drugs.

Case report

A 37-year-old white woman police office worker (weight 66.0 kg) was referred to hospital because of tachycardia and hypertension poorly responding to antihypertensive drugs. Repeated measurements of urinary catecholamines gave normal results. Investigations, including a renal arteriogram, showed a severe stenosis of the right renal artery. Plasma renin activity was two and a half times higher in the right than in the left renal vein, confirming the diagnosis of renovascular hypertension.

Treatment—in an attempt to determine the degree of angiotensin dependence of the patient's blood pressure saralasin acetate was infused. The patient had been off all antihypertensive medication for two weeks. The evening before the saralasin test she received 80 mg frusemide orally. No salt intake was allowed until after the test. Frusemide induced a diuresis of 3.5 litres and a sodium loss of 350 mmol (mEq). The patient had been recumbent for one hour when the intravenous saralasin infusion was started at a dose of 10 µg/kg/min. Blood pressure fell from an average control level of 189/138 mm Hg to 163/120 mm Hg during the second half of the infusion and returned to preinfusion levels within 30 minutes of the end of the saralasin infusion (see figure). The patient was then placed on a diet providing

a daily sodium intake of 110 mmol. From the day of the first study she received diuretics (100 mg hydrochlorothiazide and 10 mg amiloride daily) and at the end of the fourth day another oral dose of 80 mg frusemide. The saralasin infusion was repeated on the morning of the fifth day. In addition to the sodium loss of 350 mmol induced by the first dose of frusemide the further diuretic medication induced an additional negative sodium balance of 90 mmol (mEq). Blood pressure before the start of the second saralasin infusion was lower (178/131 mm Hg) and plasma renin activity (201.0 µg/l/3 h) and plasma angiotensin II level (186 ng/l) were higher than before the first infusion (plasma renin activity 88.0 µg/l/3 h; plasma angiotensin II 63 ng/l).

Adverse effect—The blood pressure fell again a few minutes after the start of the infusion. It continued to decrease during the second half of the infusion and was 135/98 mm Hg 25 minutes and 125/90 mm Hg 28 minutes after the start (see figure). The infusion was stopped. The blood pressure pressure dropped further, however, and no exact values could be recorded for two to three minutes. The patient became pale, sweated profusely, and complained of dizziness, nausea, and discomfort. A rapid infusion with plasma expanders was begun. The reversal of the hypotension, which started five minutes after the end of the saralasin infusion, seemed to occur independently of this treatment. The patient soon felt better, all symptoms disappeared, and one hour after the infusion blood pressure had returned to the pre-saralasin level. The pulse rate had been between 108 and 128 before, during, and after both saralasin tests.

Comment

Duhme *et al*³ reported a hypotensive episode during administration of the angiotensin-converting enzyme inhibitor SQ 20881 in a patient who had been sodium depleted by 80 mg frusemide and had been normotensive before the administration of SQ 20881. This patient had also been on various other antihypertensive drugs, including guanethidine, until 24 hours before the infusion. Other workers who administered saralasin or SQ 20881 after sodium depletion induced by a low-sodium diet for several days, oral or intravenous frusemide,⁴ or a combination of a low-sodium diet with a diuretic for two to four days⁵ failed to show hypotensive reactions. Our patient lost 350 mmol of sodium after a dose of 80 mg of frusemide and subsequently responded to saralasin with a significant decrease of the blood pressure. While the negative sodium balance was maintained and enhanced by an additional loss of 90 mmol during the next four days her resting blood pressure dropped slightly but remained considerably hypertensive. The response to the second saralasin dose, which led to severe hypotension, seems to show, together with the extremely high plasma renin activity and plasma angiotensin II level before the second test, that under conditions of chronic volume depletion her raised blood pressure became almost exclusively renin-angiotensin dependent.

Not only patients on vasodilating agents but also patients who are vigorously volume depleted are at risk of hypotension during blockade of the renin-angiotensin system. These patients should be excluded from screening programmes using saralasin for identifying cases of angiotensin-dependent hypertension. Careful monitoring of every patient receiving saralasin is necessary.

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Blood pressure during saralasin infusion (10 µg/kg/min) after 80 mg frusemide (upper diagram) and after four days' diuretic treatment (100 mg hydrochlorothiazide and 10 mg amiloride daily) and a single additional dose of 80 mg frusemide (lower diagram).

¹ Brunner, H R, *et al*, *Lancet*, 1973, 2, 1045.

² Pettinger, W A, and Keeton, K, *Lancet*, 1975, 1, 1387.

³ Duhme, D W, *et al*, *Lancet*, 1974, 1, 408.

⁴ Streeten, D H P, *et al*, *Circulation Research*, 1975, 36, suppl No 1, p 1.

⁵ Gavras, H, *et al*, *New England Journal of Medicine*, 1974, 291, 817.

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