Rupture of a cerebral aneurysm associated with nifedipine treatment

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Summary: We describe rupture of a cerebral arterial aneurysm in a 32 year old hypertensive woman following the introduction of nifedipine treatment. It is suggested this relationship is causal rather than co-incidental and mediated through cerebral arterial vasodilatation.

Introduction

Hypertension is a modifiable risk factor for the rupture of cerebral arterial aneurysms. We report a case where antihypertensive drug treatment may paradoxically have precipitated subarachnoid haemorrhage through rupture of a berry aneurysm.

Case report

A 32 year old woman with hypertension and asthma was being treated with bendrofluazide 10 mg/day, bethanidine 50 mg three times daily, potassium supplements and inhaled bronchodilators. No underlying cause had been found for the hypertension which had been present since the age of 6 years old. The blood pressure in clinic was 156/104 mmHg and diastolic pressures over the previous year ranged between 100 and 106 mmHg. She complained of dry mouth, stuffy nose and postural dizziness so the bethanidine dose was reduced to 50 mg twice daily with a view to gradually withdrawing it. Bendrofluazide was stopped and nifedipine 'retard' 20 mg twice daily started. The first nifedipine tablet produced mild headache but after the second she developed a severe headache, vomiting and photophobia. On admission to hospital her blood pressure was 160/100 mmHg and she had neck stiffness but no focal neurological signs. Lumbar puncture revealed uniformly blood-stained cerebrospinal fluid. Four vessel angiography showed a right posterior communicating artery aneurysm. Despite good collateral flow through the circle of Willis on angiogram, she developed a dense left hemiparesis following right carotid artery ligation. Recovery was

slow but she eventually regained independence and mobility.

Comment

This patient suffered a subarachnoid haemorrhage associated with change of her antihypertensive drugs. Blood pressure may rise rapidly to pretreatment levels after sudden cessation of bethanidine therapy (Goldberg *et al.*, 1977) but the bethanidine dose was reduced by only 50 mg daily and blood pressure on admission was similar to the recent clinic measurement. It is highly unlikely that stopping bendrofluazide would affect blood pressure within such a short time. If a drug was responsible, nifedipine seems a possible candidate but the mechanism appears to be independent of blood pressure change.

Nifedipine has important vasodilating actions on both systemic and cerebral arteries (Aboul-Khair *et al.*, 1981; Brandt *et al.*, 1983). Increased cardiac output and cerebral blood flow have been described. Despite this, cerebral ischaemia presenting as stroke or blindness has been reported on starting nifedipine (Nobile-Orazio & Sterzi, 1981; Pitlik *et al.*, 1983). These episodes may have been due to cerebral arterial 'steal' phenomena in pre-existing atheromatous cerebrovascular disease.

Subarachnoid haemorrhage associated with nifedipine has not been described but could be causally related. Theoretically, rupture of intracranial aneurysms may follow cerebral vasodilatation. Vasodilatation reduces peripheral resistance and arterial cushioning function. It also increases arterial wall stress (Laplace's law), steady state and pulsatile blood flow (O'Rourke, 1982; Safar *et al.*, 1983). These changes would increase the likelihood of aneurysmal rupture particularly if blood pressure does not fall.

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Nifedipine also reduces arterial vasoconstriction in response to pressor agents and decreases platelet aggregation. The latter may be important in the control of bleeding and rebleeding in subarachnoid haemorrhage (Gill *et al.*, 1985). However, nimodipine (a calcium antagonist 'selective' for cerebral arterial smooth muscle) may reduce vascular spasm associated with subarachnoid haemorrhage without further intracranial bleeding (Allen *et al.*, 1983).

The possibility of nifedipine predisposing to aneurysmal rupture may not be a feature of all vasodilators. Unlike hydralazine and nitroglycerine, nifedipine and enalapril dilate both the large and small

arteries (Safar *et al.*, 1983) reducing total peripheral resistance and increasing cerebral blood flow (Bertel *et al.*, 1983). We have seen subarachnoid haemorrhage in a young hypertensive man following treatment with the angiotensin converting enzyme inhibitor enalapril but were unable to obtain post-mortem evidence to confirm the presence of a cerebral aneurysm.

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