

Supervised drug administration in patients with refractory hypertension unmasking noncompliance

Cornelius C Cronin, Thomas M Higgins, Michael B Murphy, J Barry Ferriss

Summary

Noncompliance with medication is common, particularly in asymptomatic conditions such as hypertension that require long-term treatment, and is often unsuspected. We describe two patients with refractory hypertension in whom non-compliance was confirmed by a precipitous fall in blood pressure when antihypertensive medications were given under direct supervision.

Keywords: hypertension, compliance

Failure to comply with drug therapy is most often present in chronic asymptomatic conditions that require long-term treatment. We describe two patients with refractory hypertension in whom compliance was assessed by administering medication under close supervision.

Case reports

Case 1

A 38-year-old woman was referred for investigation and management of refractory hypertension. Hypertension had been diagnosed nine years previously. Two years before referral, she had suffered a left-sided hemiparesis, from which she had made a good recovery. Investigations including renal arteriography in another centre had not revealed a cause of secondary hypertension. On examination, she was thin. Blood pressure averaged 170/120 mmHg. Pulse rates ranged from 60 to 90 beats/min. Ambulatory blood pressure monitoring confirmed persistent hypertension, without a nocturnal dip. Despite being prescribed a potassium-sparing diuretic and an angiotensin-converting enzyme inhibitor, plasma potassium concentrations were low to normal and occasionally sub-normal. Appropriate investigations for causes of secondary hypertension were again negative.

Noncompliance with medication was suspected because of refractory hypertension despite treatment with multiple drugs and because plasma potassium concentration was lower and pulse rate higher than expected from the known action of prescribed medications. She was admitted to hospital for further evaluation. Daily prescribed treatment at this time was propranolol 480 mg, amiloride 40 mg, slow-release nifedipine 120 mg, methyldopa 2 g, lisinopril 40 mg, and doxazo-

sin 16 mg. Blood pressure remained persistently raised. On the eighth day, she was given, under strict supervision, propranolol 120 mg, amiloride 20 mg, lisinopril 40 mg and doxazosin 4 mg. Soon after, there was an abrupt fall in both pulse rate and blood pressure (figure 1), with near-syncope on standing. She required intravenous fluid to maintain blood pressure. Some weeks later she admitted to long-time nonadherence with the prescribed drug regimen. As an out-patient, however, blood pressure control remains poor.

Case 2

On attending her general practitioner, a 37-year-old woman was found to be hypertensive. She had recently gained 18 kg in weight. She was referred to a local hospital where investigations for secondary hypertension were negative. Blood pressure control proved difficult and she was referred to this hospital. Investigation for secondary hypertension was again negative. At a time when prescribed medications were bendrofluazide 5 mg, atenolol 100 mg, amlodipine 10 mg, enalapril 40 mg and doxazosin 16 mg daily, blood pressure levels remained persistently elevated. She denied noncompliance. She was admitted for further evaluation. After several days in hospital, she was given under direct supervision bendrofluazide 5 mg, atenolol 100 mg, amlodipine 10 mg and enalapril 20 mg. Pulse and blood pressure both rapidly fell (figure 2). She was symptomatic, with lightheadedness and

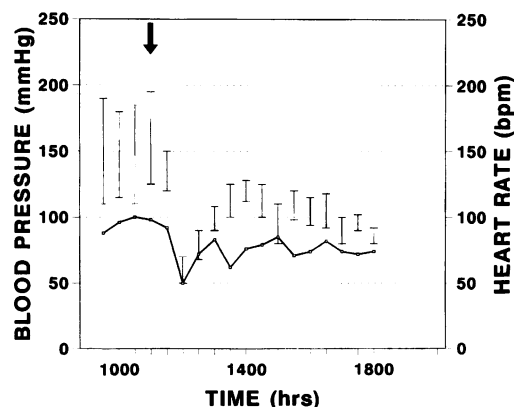


Figure 1 Blood pressure and heart rate response to the supervised administration of medication in patient 1. The bars denote blood pressure and the continuous line heart rate. The arrow indicates the time medications were given

University Hospital,
Wilton, Cork, Ireland
Department of
Medicine
CC Cronin
TM Higgins
JB Ferriss
Department of
Clinical
Pharmacology
MB Murphy

Accepted 17 June 1996

sweating, and she required intravenous fluid. Thereafter, blood pressure control was satisfactory in hospital taking bendrofluazide 5 mg and enalapril 5 mg daily under supervision. She continued to deny noncompliance. Blood pressure control has been inadequate on out-patient follow-up.

Discussion

Noncompliance with antihypertensive drug therapy is a significant problem¹ and often unsuspected,² clinicians tending to overestimate compliance.³ Available methods of detection are limited.⁴ Direct methods, such as measurement of drug or drug metabolites in biological fluids, are unsatisfactory due to the poor correlation between blood levels of many antihypertensive drugs and therapeutic efficacy, and are not generally available. Monitoring the biological response to drugs may provide clues about compliance, as, for example, in patient 1 whose heart rate and plasma potassium concentration failed to behave as expected from the known action of the medications she was prescribed. Assessing compliance in this way is, however, compromised by physiological diversity among patients. Blood pressure control itself may be used as a measure of compliance but many factors other than compliance determine blood pressure response to medication. Methods such as pill counts and prescription refill records, although relatively insensitive, are highly specific and will diagnose a proportion of cases.

Administration of medication under direct supervision may, as in the cases described, be revealing. Recent authoritative reviews of non-compliance in hypertensive patients contain little⁵ or no⁶ reference to this method of detecting noncompliance, despite acknowl-

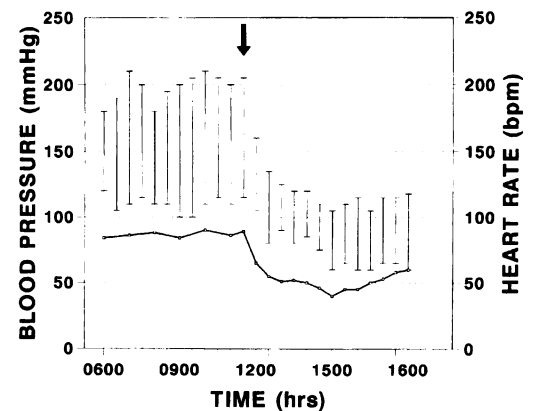


Figure 2 Blood pressure and heart rate response in patient 2 after the supervised administration of medication (symbols as in figure 1)

gement of the limitations of other methods. It is undoubtedly useful in cases when seemingly adequate therapy fails to control blood pressure in patients in whom secondary causes of hypertension have been excluded, and should arguably be an early step in the evaluation of such patients.

The dramatic blood pressure response obtained in our patients, even though they received less than their prescribed medications, suggests that this test is potentially dangerous. A precipitous fall in blood pressure may have catastrophic consequences on cerebral blood flow. Patients whose compliance is tested in this manner should receive only such medication as would be given to a newly diagnosed hypertensive patient. If a clear-cut response is not obtained, the test can be repeated using more drugs and higher dosages. If appropriate supervision is available, the test could safely be performed on a day-care basis.

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