Common and less common adverse effects of antihypertensives: a general practitioner's perspective

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Keywords: antihypertensives, common adverse effects

 S Afr Fam Pract 2012;54(2)(Suppl 1):S31-S32

Introduction

About 35% of hypertensive patients will discontinue their medication within six months,[1] and in at least 50% of cases, the reason for discontinuation relates to adverse effects and patient dissatisfaction.[2] Therefore, it is imperative that hypertension practitioners are fully cognisant of the adverse effects of antihypertensive drugs. The focus in this article will be on the six major classes of drugs, namely diuretics, angiotensin-converting (ACE) inhibitors, angiotensin-receptor blockers (ARBs), calcium-channel blockers, beta blockers and alpha blockers.[3]

The most universal adverse effect of antihypertensive therapy is hypotension, due to overtreatment. This can be subtle, and includes vague symptoms of dizziness, fatigue, tiredness, and anxiety. This is often not detected in the consulting room because of counter-regulatory measures to restore the blood pressure (BP), white-coating (especially in the elderly), and failure to perform a standing BP. Another clue to overtreatment is an unexplained increase in creatinine. Home and 24-hour ambulatory BP monitoring are useful in detecting this.

Diuretics

Thiazide diuretics are associated with a wide range of adverse effects, including hypokalaemia, hypomagnesaemia, hyponatraemia, gout, glucose intolerance, erectile dysfunction, and mild hyper-calcaemia.[4] These side-effects are generally dose related, and it is important to use low-dose diuretics in combination with other antihypertensives, especially ARBs and ACE inhibitors, which are synergistic and offset the effects on potassium. If higher doses of diuretics are required, it is essential to monitor the potassium, sodium, and uric acid.

Hypokalaemia may cause sudden death, especially if left ventricular hypertrophy (LVH) is present on an electrocardiogram (ECG).[5] The use of very high doses of thiazides, particularly in combination with amiloride (hydrochlorothiazide 50 mg, amiloride 5 mg) can cause profound and life-threatening hypokalaemia, hyperkalaemia, and hyponatraemia. Hyponatraemia may cause central pontine myelenois if corrected too rapidly. It is strongly recommended that hypertension practitioners use this drug only in half dose. It is also mandatory to measure uric acid prior to starting thiazides, as patients with hyperuricaemia are at high risk of developing gout, which may be treated with nonsteroidal anti-inflammatory drugs (NSAIDs), with consequent poor BP control. Thiazides must be avoided in patients taking lithium, because of a very high risk of lithium toxicity.

Aldosterone antagonists can cause life-threatening hyperkalaemia, especially in patients with chronic kidney disease (CKD) and concomitant use of ACE inhibitors and NSAIDs. Other side-effects include gynaecomastia, breast tenderness, menstrual irregularities, gastric ulcers, and erectile dysfunction. Generally, these complications can be avoided by using low doses (50 mg maximum), avoiding their use in high-risk situations, e.g. in the presence of CKD, and avoiding the use of NSAIDs.

ACE inhibitors

ACE inhibitors are generally well tolerated, but these drugs can cause a dry irritating cough, life-threatening angioedema (rarely), a dry metallic taste in the mouth, neutropenia (captopril only), and acute renal dysfunction (especially in patients with intercurrent illness causing dehydration, and bilateral renal artery stenosis; or in combination with NSAIDs and hyperkalaemia, especially in diabetics with CKD). Black patients are at increased risk of angioedema, as well as those with significant allergies and with a prior history of angioedema.

Angiotensin-receptor blockers

The side-effect profile for ARBs is very similar to that of ACE inhibitors, except for the coughing, angioedema, and the metallic taste. ARBs remain the best tolerated medication in practice.

Calcium-channel blockers

The most common side-effect of calcium-channel blockers is peripheral oedema, especially in women. This is dose related, and can be avoided by combining with an ACE inhibitor or ARB. Certain calcium-channel blockers, e.g. lercanidipine, cause less oedema. Dihydropyridine (DHP) calcium-channel blockers (amlodipine or nifedipine) are also associated with headaches, palpitations, flushing, gum hypertrophy, heart failure, constipation, alopecia, and allergic drug reactions. Non-DHP calcium-channel blockers, e.g. verapamil and diltiazem, have similar side-effects, except that the flushing is less severe and the constipation worse. Additionally, they may cause bradycardia and heart block, especially if combined with beta blockers, and require electrocardiographic monitoring.

Beta blockers

Beta blockers have a wide range of side-effects, including bradycardia, wheezing or unmasking of asthma, masking of hypoglycaemia, sleep disturbances, fatigue, exercise intolerance, erectile dysfunction, glucose intolerance, worsening of peripheral vascular disease, drowsiness, Raynaud's phenomenon, heart failure, dyslipidaemia, and precipitation of angina with sudden withdrawal. Practically, it is best to use the most selective β blockers or carvedilol (non-selective with α-blocking effects). Use cautiously in patients with a prior history of asthma in childhood, and in diabetics who are prone to hypoglycaemia.

Alpha lockers

Alpha blockers are useful drugs in patients with prostatic hypertrophy and resistant hypertension. The most common side-effect is postural hypotension (particularly in the elderly), and precipitation of heart failure. This is a problem in short-acting drugs, e.g. prazosin and doxazosin, and it is strongly recommended that the slow-release preparations of doxazosin only are used to lessen the risk. Beneficial side-effects include improved lipid profile and sexual function.

Conclusion

Adverse effects of antihypertensive drugs are common, and can lead to discontinuation of therapy. By being cognisant of these side-effects, the hypertension practitioner can tailor his or her therapy to suit the individual patient. Using low doses of drugs in combination is also a good strategy to avoid side-effects.

References

1. Vrijens B, Vincze G, Kristanto P, et al. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. BMJ. 2008;336(7653):1114-1117.
2. Bloom BS. Continuation of initial antihypertensive medication after 1 year of therapy. Clin Ther. 1998;20(4):671-681.
3. Düsing R, Weisser B, Mengden T, Vetter H. Changes in antihypertensive therapy: the role of adverse effects and compliance. Blood Press. 1998;7(5-6):313-315.
4. South African Medicine Formulary. 9th ed. Rondebosch: Health and Medical Publishing Group; 2010.
5. Baseline rest electrocardiographic abnormalities, antihypertensive treatment, and mortality in the Multiple Risk Factor Intervention Trial. Am J Cardiol. 1985;55(1):1-15.