Drug-induced causes of secondary hypertension

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Resistant hypertension is a blood pressure that remains above the treatment goal despite use of optimal doses of three antihypertensive drugs of different classes including a diuretic (1). Patients with resistant hypertension should be screened for causes of secondary hypertension (2). Common causes of secondary hypertension include renal parenchymal disease (1), renovascular disease (3), dug-induced causes (4), pregnancy (5), primary aldosteronism (6), and obstructive sleep apnea (7). Uncommon causes of secondary hypertension include acromegaly, hyperthyroidism, hypothyroidism, hyperparathyroidism, Cushing syndrome, apparent mineralocorticoid excess, pheochromocytoma/paraganglioma, carcinoid syndrome, congenital adrenal hyperplasia, coarctation of the aorta, and neurological causes (2). This article will discuss some of the drug-induced causes of secondary hypertension.

Excessive dietary sodium intake contributes to resistant hypertension by directly increasing blood pressure and by blunting the efficacy of most classes of antihypertensive drugs (8). This effect is especially pronounced in salt-sensitive persons such as older persons, blacks, and those with chronic kidney disease (1). Sodium-containing antacids should be avoided. Excessive alcohol use raises blood pressure and can cause resistance to antihypertensive drug therapy (4,9). Alcohol use should be restricted to ≤2 drinks daily for men and ≤1 drink daily for women (9). There is no difference in risk between beer, wine, and liquor (9). A meta-analysis of five studies in persons with hypertension showed that ingestion of 200 to 300 mg of caffeine caused an increase in blood pressure of 8.1/5.7 mm Hg, and the increase in blood pressure lasted for ≥3 hours (10). Persons with uncontrolled hypertension should avoid caffeinated beverages. Nicotine, cocaine, methamphetamine, and other recreational drugs which increase blood pressure should be avoided (2,9). Cocaine causes a severe increase in blood pressure, especially if the person is taking a beta blocker (4). Smoking cessation decreases systolic blood pressure (9).

Because of their widespread use, nonsteroidal anti-inflammatory drugs, aspirin, and acetaminophen are the commonest drugs in worsening control of blood pressure (1). Blood pressure is increased by both cyclooxygenase 1-inhibitors and by cyclooxygenase 2-inhibitors. Nonsteroidal anti-inflammatory drugs increase blood pressure by influencing prostaglandin production causing adverse renal effects (9). Nonsteroidal anti-inflammatory drugs also increase systemic vascular resistance by increased endothelin-1 synthesis and by altered arachidonic metabolism (9). In 9,411 patients aged 65 years and older, use of nonsteroidal anti-inflammatory drugs increased the risk of starting antihypertensive drug treatment 1.55 times if low daily doses were used, 1.64 times if medium daily doses were used, and 1.82 times if high daily doses were used (11). Nonsteroidal anti-inflammatory drugs also blunt the blood-pressure lowering of antihypertensive drugs including diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and beta-adrenergic blockers (12,13). Nonsteroidal anti-inflammatory drugs should be avoided if possible in persons with hypertension and other analgesics used depending on the indication.

Amphetamine, methylphenidate dexmethylphenidate, and dextroamphetamine used to treat attention-deficit/hyperactivity disorder in children and adolescents may cause an elevated blood pressure (14). Behavioral therapies should be considered for the treatment of this disorder. Antidepressants such as monoamine oxidase inhibitors, serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressants may cause an elevated blood pressure (4).

Persons taking monoamine oxidase inhibitors must avoid foods and beverages containing high levels of tyramine such as liver, alcohol beverages, and aged cheeses or they may have a hypertensive crisis. Atypical antipsychotics such as clozapine and olanzapine may also cause an elevated blood pressure (15). Their use should be limited when possible.

Sympathomimetics such as the decongestants containing phenylephrine or pseudoephedrine may cause an elevated blood pressure (2). Alternative therapies such as nasal saline, intranasal corticosteroids, and antihistamines should be considered. Appetite suppressants may cause an elevated blood pressure (2). Herbal supplements such as ephedra, St John's wort, and yohimbine should be avoided since they have no clinical efficacy and may cause an elevated blood pressure (2).

Systemic corticosteroids such as dexamethasone, fludrocortisone, methylprednisolone, prednisone, and prednisolone may cause an elevated blood pressure (4). The increase in blood pressure is dose dependent. Alternative ways of administration of these drugs such as inhalation or topical use should be considered. Mineralocorticoids including licorice, carbenoxolone, 9-alpha fluorocortisol, ketoconazole, and carbenoxolone may cause an elevated blood pressure (4,16). The increase in blood pressure caused by these drugs is dose-dependent and is associated with hypokalemia, metabolic alkalosis, and a reduction in plasma renin activity and aldosterone levels (4,9).

Estrogens, androgens, and oral contraceptives may cause an increase in blood pressure (2,4,9). Oral contraceptives should not be used in women with uncontrolled hypertension (4). Low-dose ethinyl estradiol (20–30 mcg) agents should be used (4). Alternative methods of birth control should be used.

Immunosuppressants may cause an increase in blood pressure (2,4,9,17,18). Meta-analyses of randomized trials have demonstrated that cyclosporine treatment is associated with a higher incidence of hypertension than is treatment with tacrolimus (17,18).

Chronic use of recombinant human erythropoietin may cause hypertension (19). Mechanisms for the erythropoietin-induced hypertension include increase in hematocrit and erythrocyte mass, increased sensitivity to endogenous vasopressors, dysregulation of production or responsiveness to endogenous vasodilatory factors, a direct vasopressor effect, and stimulation of vascular cell growth (19). A sympathomimetic hypertensive crisis may be induced by abruptly stopping clonidine or other sympatholytic drugs or by using cocaine, amphetamines, phencyclidine, or monoamine oxidase inhibitors (20).

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Footnote

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