



Can Common Blood Pressure Medications Cause Diabetes?

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High blood pressure, or hypertension, is a major risk factor for cardiovascular disease. In the United States, approximately one in three adults has high blood pressure, totaling an estimated 72 million people. Additionally, more than half of Americans over the age of 60 have hypertension.¹

High blood pressure can be caused by a number of factors including hormones, kidney disease, and cardiovascular disorders. Blood pressure increases due to increased force of the contraction of the heart and increased peripheral resistance in the blood vessels. In the renin-angiotensin system, the enzyme renin activates the hormone angiotensin-1, which is then converted to angiotensin-2 by angiotensin-converting enzyme (ACE). Angiotensin-2 increases blood pressure by increasing sodium and water retention from the kidneys and constricting the smooth muscle around the arteries. Additionally, nitric oxide is a molecule that is produced in the endothelial lining of blood vessels where it locally causes the smooth muscle surrounding the blood vessels to relax. Sufficient production of nitric oxide is required to decrease peripheral resistance of the blood vessels. Peripheral resistance can also be increased as a result of hardening of the arteries due to calcium deposits and atherosclerotic plaque formation. There is also research regarding parathyroid hypertensive factor (PHF), a substance released from the parathyroid gland that is believed to increase blood pressure by interfering with normal calcium channel activity in vascular smooth muscle cells. Elevated PHF levels correlate with hypertension, especially in low-renin, salt-sensitive patients.²⁻⁴

There are several types of pharmaceutical drugs commonly prescribed to manage high blood pressure, in addition to diet and lifestyle modifications. Diuretics, or water pills, are used to flush excess fluid and sodium from the body to decrease the amount of fluid pumped by the heart. Beta-blockers are used to decrease the rate and force in which the heart pumps blood, and alpha-blockers decrease nerve impulses that constrict blood vessels. Calcium channel blockers inhibit calcium from entering the muscle cells of the heart and blood vessels,

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allowing blood vessels to relax. Angiotensin converting enzyme (ACE) inhibitors suppress the hormone angiotensin-2, which causes water retention and blood vessels to narrow.⁵

It is interesting that death caused by coronary artery disease and sudden death is not significantly reduced by the use of anti-hypertensive medications in hypertensive patients, despite the evidence that hypertension is a major risk factor for heart attacks.⁶ Some researchers suggest that this is due to adverse metabolic effects caused by the pharmaceuticals that counteract the benefits of lower blood pressure.⁶ For example, diuretics disrupt electrolytes causing low potassium, magnesium, and sodium, and may increase uric acid. Thiazide diuretics are also associated with a decline in kidney function.⁷ Both diuretics and beta-blockers interfere with blood glucose and lipid metabolism, and ACE inhibitors can elevate potassium.⁸

Some of the most concerning findings indicate that thiazide diuretics, considered the first-choice drug for hypertension, are associated with an increased risk of diabetes. In one study, non-diabetic subjects age 60 or older with systolic hypertension were treated with the thiazide diuretic chlorthalidone or a placebo. The results showed that this diuretic significantly decreased levels of serum potassium, known as hypokalemia, and this correlated with a significant increase in diabetes. In fact, the study showed that for each 0.5 milliequivalent-per-liter (MEq/L) decrease in serum potassium, there was a 45 percent increased risk of developing diabetes.⁹ Diabetes mellitus and hypertension each independently confer increased cardiovascular risk, and that risk is much greater when the diseases coexist.

According to the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, thiazide-type diuretics should be used as the first choice therapy for most patients with hypertension, despite the data from the large ALLHAT trial, which showed that thiazide-type diuretics cause hypokalemia, glucose intolerance, and diabetes. The study showed a significant 43-65 percent higher risk of new-onset diabetes with the diuretic chlorthalidone compared with a calcium channel blocker (30 percent) and an ACE inhibitor (18 percent). The researchers justified their recommendation to use thiazide-type diuretics as the first choice therapy for most patients with hypertension based on the data that the greater incidence of diabetes did not translate into more

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cardiovascular events. However, other researchers suggest that drawing such a conclusion ignores the morbidity and mortality associated with diabetes over decades, and not the short 2-6 year time frame examined in the ALLHAT study.¹⁰⁻¹¹

Another study found a similar association between anti-hypertensive drugs and diabetes. This long-term study found that 20.4 percent of hypertensive subjects treated with anti-hypertensive medications developed diabetes, and new-onset diabetes correlated with a significantly increased risk for stroke, myocardial infarction, and mortality.¹² Other studies have shown that the mean fasting glucose levels increased with thiazide-type diuretics, a calcium-channel blocker, or ACE inhibitor measured after 4.9 years,¹³ and patients with hypertension who were taking beta-blockers had a 28 percent higher risk of developing type 2 diabetes.¹⁴

In addition to diabetes, anti-hypertensive medications are associated with adversely impacting lipid profiles. Studies have shown that beta-blockers reduced the ratio of beneficial high-density lipoprotein (HDL) to total cholesterol by 11.7 percent and increased serum triglyceride levels by 25.8 percent.¹⁵ Diuretics can cause an increase in total and low-density lipoprotein (LDL) cholesterol and triglyceride levels while beta-blockers can decrease HDL cholesterol and increase triglyceride levels.¹⁶ Some beta-blockers also have been found to decrease levels of CoQ10.¹⁷

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