Antihypertensive Medications and Weight Gain

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Patients receiving antihypertensive drugs justifiably raise concerns about adverse effects. Weight gain is a common clinical problem, and patients may ask, "Will [or did] this antihypertension medication cause me to gain weight?" The answer to this question is available, but some practitioners may be unaware of the data.

First, one needs to appreciate the distinction between peripheral edema and weight gain. Several antihypertensive medications cause peripheral edema—notably the calcium channel antagonists—by redistributing body water to the extravascular space, but they do not usually cause actual weight gain. Thiazide diuretics and angiotensin-converting enzyme inhibitors typically cause a transient loss of 1–2 kg body weight in the first 6–8 weeks of therapy secondary to salt and water diuresis. One class of antihypertension medications that does cause true weight gain is the β blockers.

In the 1980s and 1990s, randomized trials of β blockers for the treatment of high blood pressure or as therapy for postmyocardial infarction reported weight gain in the groups treated with β blockers. For example, the United Kingdom Prospective Diabetes Study Group (UKPDS) reported a mean weight gain of 3.4 kg in the atenolol group vs. 1.6 kg in the captopril group over 9 years of observation,[1] a net change of 1.8 kg or 4 lb. The trials of β blockers were not designed specifically to evaluate weight gain; however, a large retrospective study of the data prospectively collected in the Beta Blocker Heart Attack Trial demonstrated mean weight gain of 2.3 kg in the propranolol arm vs. 1.2 kg in the placebo arm,[2] a net of 1.1 kg or about 2.5 lb. This weight gain was sustained after 3 years and independent of age, sex, degree of physical activity, and discrepancies in the use of diuretics. A recently published review demonstrated significant weight gains of 0.5–3.4 kg (1–2.5 lb) in the β blocker groups in six of eight prospective trials.[3] The weight gains occurred in the first months of therapy, were sustained, and were independent of demographic variables.

There are multiple proposed mechanisms of weight gain during therapy with β blockers. These can be divided into two broad categories: altered metabolism and decreased physical activity. The first category includes reduction in basal metabolic rate, reduction in the thermogenic response to meals, increased insulin resistance, and inhibition of lipolysis. The latter category includes diminished exercise tolerance secondary to fatigue or dyspnea and decreased purposeless movements, also known as nonexercise-associated thermogenesis.

What are the clinical implications of these observations? The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure makes no reference to this phenomenon and, consequently, makes no recommendations regarding the selection of antihypertensive agents in obese patients with hypertension.[4] It is clear that the benefits of β blockers in patients with conditions such as congestive heart failure, cardiac arrhythmias, and ischemic heart disease outweigh the potential risk of modest weight gain. Nevertheless, in obese patients with hypertension (particularly with the metabolic syndrome) who lack clear indications for β blockade, it might be prudent to select an antihypertensive agent from a different class for the initial treatment of hypertension.

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