Suboptimal Adherence to Antihypertensive Treatment: Causes and Management

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Abstract: Suboptimal adherence to antihypertensive treatment is very common and is associated with poor control of blood pressure and increased risk for cardiovascular events. Therefore, frequent evaluation of compliance is essential in all hypertensive patients. Simplifying treatment regimens, using fixed-dose combinations and long-acting agents improves adherence, facilitates achievement of treatment targets and reduces cardiovascular morbidity and healthcare expenditures. Accordingly, physicians should be educated to implement these changes in hypertensive patients, particularly in those who require multiple antihypertensive agents to achieve blood pressure controls and in those who receive additional medications for comorbidities.

Keywords: Hypertension, Adherence, Compliance, Fixed-dose combination, Cost, Cardiovascular morbidity, Compliance indices.

Hypertension is accountable for 9.4 million deaths per year worldwide. Hypertension is a major modifiable risk factor for coronary heart disease, stroke, chronic kidney disease and heart failure [1]. The American Heart Association/American College of Cardiology recently recommended an aggressive approach in the management of hypertension, characterizing as stage I hypertension systolic blood pressure [BP] > 130 mmHg and/or diastolic BP > 80 mmHg [2]. On a more conservative approach, the European Society of Cardiology/European Society of Hypertension consider as stage I hypertension systolic BP > 140 mmHg and/or diastolic BP > 90 mmHg [3].

The first step for the management of hypertension consists of adoption of a healthier lifestyle, i.e. regular exercise, reduction in sodium intake, weight loss decrease in alcohol consumption and smoking cessation. In blood pressure targets are not achieved with lifestyle changes, antihypertensive treatment should be initiated and continued for life [1 - 3]. Antihypertensive treatment has been consistently shown to reduce cardiovascular morbidity and mortality [4].

Despite the established benefits of antihypertensive treatment, a considerable proportion of patients with hypertension do not adhere to the prescribed antihypertensive therapy. It has been reported that only 30% of hypertensive patients continue to receive their antihypertensive treatment at 1 year after treatment initiation [5]. Moreover, most patients discontinue treatment within the first 3 months [5]. A recent study reported that one in every 8 patients filled-in only one prescription of antihypertensive agents [6]. These rates have remained unchanged during the last decade, despite the increasing rates of awareness and management of hypertension [7]. Of note, even patients with resistant hypertension who undergo renal denervation show poor adherence to treatment [8 - 11] Table 1. Interestingly, it has been reported that a substantial proportion of patients take higher doses of antihypertensive agents than those recommended, a practice which is also associated with higher risk for cardiovascular events [12].

Several factors contribute to the low rates of adherence to antihypertensive treatment. First, most patients require multiple agents to achieve BP targets and compliance declines with the increase in number of prescribed medications [13]. Accordingly, the use of fixed compositions has been consistently shown to improve compliance to antihypertensive therapy [14 - 17]. Fixed combinations also appear to reduce BP more than free combinations [16, 17]. Healthcare costs and cardiovascular morbidity also appear to be reduced by the use of fixed combinations [18, 19]. Reducing the complexity of the drug therapy by prescribing long-acting agents taken once daily also has favorable effects on adherence [18 - 21]. Among patients treated with 3 antihypertensive agents, reducing this number to 2 had a positive impact on adherence [22]. Moreover, combining antihypertensive agents with a statin and aspirin in a single pill also improves adherence [23]. In addition, initiation of antihypertensive treatment simultaneously with lipid-
lowering therapy also results in better compliance to both treatments, possibly because it enables patients to organize better medication refill [24]. A second important driver of low adherence is the cost of medications. Indeed, the use of generic medications is associated with better adherence [25]. Female gender, young age, low socioeconomic status and absence of comorbidities are also associated with suboptimal adherence [26]. In contrast, patients with established cardiovascular disease appear to be more compliant to antihypertensive treatment, possibly because they had better perception of their risk for a recurrent cardiovascular event [27]. Among antihypertensive classes, compliance appears to be better with angiotensin converting enzyme inhibitors and angiotensin receptor blockers [6, 15, 26]. Educating the patients about the benefits of antihypertensive treatment on cardiovascular morbidity and mortality, stressing the need for sustained adherence and addressing concerns about the safety of antihypertensive agents is also important in improving adherence. Having a schedule in medication intake and use of electronic reminders are also helpful. Regular evaluation of adherence and discussion of barriers to adherence are also important.

### Table 1. Adherence to antihypertensive treatment in patients with resistant hypertension undergoing renal denervation.

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<tr>
<th>References</th>
<th>Number of Patients</th>
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<td>8</td>
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Suboptimal adherence to antihypertensive treatments increases the risk for cardiovascular morbidity, adversely affects quality of life and increases healthcare costs [5, 15, 28]. In a recent meta-analysis of 18 studies (n = 1,356,188), a 20% increase in adherence to antihypertensive treatment was associated with a 9% lower risk of stroke [29]. In another meta-analysis of 44 prospective studies (n = 1,978,919), patients with good adherence to antihypertensive medication had 19% lower risk for cardiovascular events and 29% lower all-cause mortality than patients with poor adherence [<80% adherence] [30]. Accordingly, monitoring the patients’ compliance to treatment is essential. National healthcare databases are increasingly recognized as a useful and reliable source for evaluating the adherence to antihypertensive therapy [6, 31]. Moreover, recent consensus statements describe in detail the methods to assess adherence, which is important for obtaining consistent and comparable results from different healthcare systems [32]. Several different indices have been used to evaluate compliance to treatment [33]. A frequently used measure is the medication possession ratio (MPR), which represents the ratio of the patient’s daily supply of all medications divided by a specific period of time [15, 33, 34]. Another commonly employed index is the proportion of days covered (PDC), which represents the amount of days a drug is accessible [35, 36]. The PDC is considered more reliable than the MPR for evaluating adherence because the latter cannot distinguish between drug discontinuation, substitution and addition [37]. Several other methods are used to evaluate adherence in everyday clinical practice including estimation of adherence by physicians, self-reported adherence using questionnaires, pill counting, electronic monitoring using an electronic pillbox, direct observation of intake of antihypertensive medications, measurement of biomarkers in the plasma or the urine and detection of antihypertensive drugs or their metabolites in the urine [38].

In conclusion, suboptimal adherence to antihypertensive treatment is very common and is associated with poor control of blood pressure and increased risk for cardiovascular events. Therefore, frequent evaluation of compliance is essential in all hypertensive patients. Simplifying treatment regimens, using fixed-dose combinations and long-acting agents improves adherence, facilitates achievement of treatment targets and reduces cardiovascular morbidity and healthcare expenditures. Accordingly, physicians should be educated to implement these changes in hypertensive patients, particularly in those who require multiple antihypertensive agents to achieve blood pressure controls and in those who receive additional medications for comorbidities.

### CONSENT FOR PUBLICATION

Not applicable.

### CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES


