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COMMENTARY ARTICLE

Hypertension: Drug Adherence and Social Factors

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Introduction

Hypertension is the most prevalent cardiovascular risk factor in the world, increasing significantly with aging [1]. The treatment of arterial hypertension leads to the reduction of the risk of cardiovascular events, such as stroke and heart disease [2]. In the adult population, the prevalence of hypertension is about 30 to 45%, varying between countries [1]. In 2010, more than 1.3 billion adults age ≥ 20-years-old were hypertensive worldwide, representing an estimated global age-standardized prevalence of hypertension of 31.1%. This figure is increasing with ageing and in the developing countries [3]. In Portugal the prevalence in adults over 18 is estimated in 42.2%, higher in men (44.4% versus 40.2% in women) [2].

The diagnosis of hypertension is primarily based in the office visit's measurements. The value of 140/90 mmHg is the consensual cut-off. Values equal or higher both in systolic or diastolic blood pressure, in patients not previously medicated with antihypertensive medication, define the diagnosis [1]. Last review of the American Heart Association (ACC/AHA) guidelines for hypertension released new targets for the definition of Hypertension, starting on hypertension stage 1 if patient´s blood pressure is higher than 130-139 or 80-89 mmHg, and hypertension stage 2 is ≥ 140 or ≥ 90 mmHg [4]. This new definition is based in recent data, showing a significant increase in cardiovascular risk at lower blood pressure values, especially the SPRINT study [5]. However, these guidelines aren't consensual. They significantly increase the prevalence of people living with the diagnosis of hypertension, but not much the recommendation for antihypertensive medication treatment [6]. On the other hand, SPRINT study included high risk hypertensive patients in the enrolment, not allowing the extrapolation for general population in primary prevention. These contradictions lead several societies to reject the rational and the proposal of 2017 American Guidelines. The American Family Physician also asks for the opportunity of making the diagnosis of hypertension based on the out-of-office blood pressure readings instead of an accurate measurement made by a physician, without a clarification of the potential harms versus the net benefit of the treatment intensification [7]. The new guidelines of European Hypertension Society for the Management of Arterial Hypertension will soon be published, and hopefully they will bring some sense to this discussion. Early highlights point the need to improve the treatment of high blood pressure, leading more patients to control the hypertension, which at present is not as good as it should be. Treatment options include naturally the improvement of pharmacological approach, but non-pharmacological interventions and lifestyles modifications are crucial to achieving the targets and should be constantly reinforced. The problem is taking the patients to adhere both to pharmacological and non-pharmacological interventions [8-11].

Therefore, the aim of this article is to review critically the major determinants that interfere with non-adherence and present strategies to improve blood pressure control.

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Key Concepts of Adherence to Medications

Adherence is normally accepted as the extent to which a person's behavior corresponds with agreed recommendations from a health care provider, both in taking a medication, following a diet or executing lifestyle changes [12]. It divides in compliance, representing the patient's passive following of provider's orders, and in persistence, as the duration of time patient takes the medication, from initiation to discontinuation of therapy [13]. It has a multidimensional nature due to the different players in the problem: Patients, providers and health care system, and how they interact with each other [11].

Patients have to feel that a negative health condition is a true personal threat and that it can be avoided by the recommended action, if they can successfully take it [14]. However, several problems can interfere like psychological problems, as depression, cognitive deficit, low insight into diagnosis, especially in asymptomatic diseases. On the doctor's side, we point the poor patient-physician relationship, the inadequate follow-up plan and the side effects of treatments. Poor accessibility to care or medicines, the cost of medication, and care and missing appointments are relevant factors related to health systems' organization.

Adherence to Medications in Hypertensive Patients

We accept the concept of drug adherence as the extent to which patients take their medications as prescribed by their healthcare providers [11]. High blood pressure is the main determinant of death worldwide since a long time and we could expect that this threat was well-known by general population as everybody frequently wants to measure their blood pressure [15]. Unfortunately, the reality is far from desired. Adherence to anti-hypertensive medications depends on the patients' behaviour and expectations, the type of medication, the patient-physician relationship, the therapeutic inertia, as providers sometimes don't value properly some deviations to the blood pressure targets, the power of external sources like media, internet and friends' opinions, and several other factors [10]. Ideally, the compliance should be similar to the adherence representing the degree of obedience to the indicated treatments, pharmacological or not, aiming to lower the blood pressure to the target level, and both near 100%, meaning that all the patients respect treatment instructions, following doctors' information and prescription. However, non-adherence is very common and about half, or more, of patients don't take their medications as prescribed [16,17].

Measuring the Adherence to Medications

There is no Gold Standard method to measure drug adherence. The adherence questionnaires are indirect methods. Although frequently inaccurate and biased by patients' behaviour, they remain very valued, providing opportunities to identify patients needing counselling and to educate them according their answers [10]. Pill counting is often used in clinical trials and clinical practice [18,19]. It's more accurate than questionnaires and many times referred as standard for evaluating the adherence to medications [18]. It's based on the number of pills effectively taken, that is, the number of pills dispensed less the number of pills leftover, weighed by number of days of prescription. If the patient has to take a medication twice a day for 30 days, and the prescription has exactly the 60 pills, the number of pills remaining in the box divided by number of daily intakes retrieves the days of non-adherence [19]. However, both patients' questionnaires and pill counting may overestimate adherence to medications because they are dependent of patients report [20]. Electronic counting through a pillbox can overcome the problem, but it's expensive and so not often used. Direct methods, like direct observation of intake, utilization of plasma and urine biomarkers and urine drug detection, are better and more accurate for monitoring, but also more intrusive, and not always easy to apply in clinical practice [10].

Antihypertensive drugs are effective to lower the blood pressure and to prevent cardiovascular, cerebrovascular and renal complications and even death [21]. However, due to the asymptomatic and chronic characteristics of hypertension, non-adherence is highly prevalent, putting patients' health at risk. Attention to the adherence, using a combination of different assessment methods is likely the most effective approach to improve it [10].

Strategies to Improve Adherence to Medications in Hypertensive Patients

Pharmacological treatment is well established in different hypertension guidelines. Antihypertensive drugs proved to be cost-effective, lowering the cardiovascular risk with good security profile and tolerance. The different classes cover the physiopathology pathways of hypertension. They may be combined in single pills with fixed doses, gaining better acceptance and adherence by both patients and doctors [22]. Even since, blood pressure control is far from the ideal, mostly because of low adherence to antihypertensive drugs. The need to use combinations of several medications is an important factor. The unifactorial causality relationship has still a very relevant symbolic presence in most of population: One cause, one disease and one treatment, opposing the current multifactorial approach, that justifies the multiple and different combinations. Another factor in accounting is the drug-related side effects as fatigue, headache, peripheral oedema, cough, allergy, polyuria, erectile and libido dysfunction and metabolic changes, some of them very uncomfortable for patients [23].

The side effects profile justifies that certain medication classes, as beta-blockers and thiazide-diuretics, present lower adherence rates as compared to other classes [10]. Side-effect profile is better evaluated in monotherapy, allowing the establishment of the causal relationship, as the assignment of efficacy. However, most of hypertensive patients will need a combination of two or more drugs, seizing the synergistic effect among the different classes. Using fixed doses in single pill combinations favours higher rates of adherence [24,25]. Nevertheless, evidence shows that 25% of patients do not buy all medications prescribed by the attending physician [26] and 10% of patients often forget to take the prescribed medication on a daily basis. Also, one-third of patients discontinue initial treatment after 6 months and half of patients after one year [16,27]. Recent data suggests that non-adherence occur in 45.2% of all hypertensive patients, and reaches 83.7% in uncontrolled patients [28].

Patient-related factors are relevant determinants for non-adherence. They include lack of understanding their disease, lack of involvement in the treatment decision-making process and, more often, suboptimal health literacy. It's crucial to improve patients' expectations on the effectiveness of the treatment, dealing with previous experiences with pharmacological therapies and lack of motivation. Bad family support and loneliness are also factors that should not be forgotten [19]. The true challenge in medication adherence is to enhance patients' health literacy and to empower them to make good choices for their own health [29].

Males are more likely to show low adherence rates, as the youngers, especially in resistant hypertension [23]. Also, the presence of depression and chronic heart disease are associated to lower drug adherence [30].

Therapeutic adherence is higher in patients with better education and better knowledge about their disease, and also with greater economic income [31-33]. Adherents present better quality of life, both in their physical and their mental status [34]. Health literacy and education should be a priority in these patients and in all people [29]. Moreover, there's a 'healthy adherer effect', where patients who adhere to medications are more likely to engage in other healthy behaviour, like changes in lifestyles, which may influence their health outcomes [10]. Nurses play a very important role in educating the patients towards a better literacy [35].

Providers play an important role in non-adherence. Physician-related factors are very common, when prescribing complex drug regimens, when failing to explain effectively the benefits and harms of the medication, and when disregarding the financial burden to the patient [19]. Doctor-patient communication is crucial and should always be reinforced. The pressure of timing not always enough to make a proper consultation, the waiting time for an appointment and the technology too many times inefficient are problems relevant to medical adherence. Doctors and patients must work together, negotiating the best options in a clinical reasoning pathway towards the achieving of health outcomes, defined and accepted by both. Simplifying the regimen characteristics, imparting knowledge and literacy, modifying patient beliefs and expectations, improving the communication with the patients, leaving the bias and evaluating continuously the process are strategies to enhance adherence which may be applied to patient care settings [36].

Several issues are easy to implement in clinical practice. Lowering the intake frequency is many times possible, putting all medication, or at least the most, at the same time [37]; when we need to intensify the regimen, it's possible to join several drugs in one single pill, with advantages in adherence [22]; providing a good channel for communication with patients, addressing benefits and potential harms of different options both pharmacological and non-pharmacological; and checking regularly the rate of adherence, using the different strategies already focused. Also, an effective interaction between different levels of health care, with exchanging of information in real-time, facilitates the adherence to medications [19].

Adherence to medications is a multifactorial phenomenon, hard to explain in its globality. An intervention that works in one patient may not work in another, leading to the need of combining several strategies, [10] in a personalized way, putting the patient in the center of the system.

Conclusion

Arterial hypertension is the most important risk factor for cardiovascular diseases [1]. Improving blood pressure control is crucial to reduce the cardiovascular morbidity [2], which remains the main cause of death worldwide [38]. In Portugal, we saw a good evolution since the PAP study, in 2001 [39], to the PHYSA study, in 2011 [2], improving the number of patients that are aware of their high blood pressure and the number of patients that had their blood pressure controlled (< 140/90 mmHg). The causes aren't sufficiently established but the improvement of the attention given to blood pressure, especially in primary care, both by doctors and by patients, the vulgarization of single pill associations with 2 or 3 drugs and the reduction in salt consumption in population are certainly relevant factors. Nevertheless, although we have good drugs for controlling of high blood pressure, we still fail in many patients.

Charles Koop once said that no drug is effective if patients don't take it. (C. Everett Koop, MD, US Surgeon General, 1985).

This is crucial to get better results in treatment of arterial hypertension. Patient`s responsibility is the way

to achieve it and it depends on improving education and literacy, leading to better skills and to higher empowerment [29,40].

More than lowering the targets for blood pressure, it's necessary to look for the determinants of non-adherence and fight them, both in lifestyles and in medication, ensuring the lighten of the burden of hypertension in patients, in health care services and in the health systems.

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All authors contributed equally to the design, writing and discussion of the present manuscript.

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