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Adherence to Treatment in Hypertension

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Abstract

The lack of adherence to treatment in hypertension affects approximately 30 % of patients. The elderly, those with several co-morbidities, social isolation, low incomes or depressive symptoms are the most vulnerable to this problem. There is no ideal method to quantify the adherence to the treatment. Indirect methods are recommended in clinical practice. Any intervention strategy should not blame the patient and try a collaborative approach. It is recommended to involve the patient in decision-making. The clinical interview style must be patient-centered including motivational techniques. The improvement strategies that showed greater effectiveness in the compliance of hypertension treatment were: treatment simplification, appointment reminders systems, blood pressure self-monitoring, organizational improvements and nurse and pharmacists care. The combination of different interventions are recommended against isolated interventions.

Keywords

Hypertension • Patient compliance • Medication adherence

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1 Introduction

High blood pressure (hypertension) is a chronic disease. Several measures, such as habits of life, diet and medication, are required for its control. It is widely known that the greater efficacy of nowadays available treatments does not correspond with an increase in the number of controlled patients. So, it is important to measure compliance and study which factors might influence it. Approximately 50 % of patients with a hypertension prescription will stop it during the first year and only 50–66 % of the remaining patients will keep with the treatment prescribed. As a result, only 25–34 % of patients with hypertension will have a good control of their blood pressure (BP) figures (Morris et al. 2006). The lack of adherence to treatment is a common phenomenon, especially in chronic conditions. According to data from the World Health Organization (WHO), adherence to long-term treatment of chronic diseases in developed countries is around 50 %, with rates even lower in developing countries. Therefore, non-compliance of the chronic treatments and their clinical and economic consequences is considered a priority public health issue (WHO 2004).

There is no personality profile associated with the low-adherent patient to medical treatments. On the other hand, non-adherence is difficult to predict and the point of view expressed by the health-professionals does not correlate with the actual compliance. In fact, it is no more accurate than throwing a coin in the air (Medding et al. 2012). Patients with hypertension have characteristics that favors poor compliance (Table 1). It is often difficult to follow the health professional recommendations in chronic and asymptomatic problems. It is hard to become aware of the need of a long-term treatment. Hypertension diagnosis at the age of forty, can mean a loss of vigor and vitality for the patient. Sometimes it can cause a denial reaction and an economic and social burden that hinders acceptance of treatment (Kaplan et al. 2016). Curiously, the adherence of the prescription is unrelated to the implementation of lifestyle changes. So, the decision to quit smoking or doing exercise is not associated with greater adherence to the medication. Patients want to know why should they take medication, which benefits and side effects can be expected, the cost and what would happen if they do not follow the therapeutic guidelines. Health professionals, in general, communicate poorly with their patients and provide little information about medical prescriptions (Fuster 2012).

Table 1 Major predictors of non-adherence to treatments

Dependent on the Patient
Chronic process
Asymptomatic disease
Lack of knowledge of the disease by the patient
Lack of confidence in the benefit of the treatment by the patient
Missing scheduled appointments
Presence of psychological problems
Cognitive impairment
Social isolation
Dependent on the Treatment
Complexity or long duration of treatment
Adverse effects of medication
Inadequate patient-physician relationship
Fragmented attention: lack of coordination
Absence of scheduled periodic appointments
Cost of medication

2 Consequences of Non-compliance

Several results from adherence studies are available. Thus in a study involving more than 18,000 patients followed during 4.6 years, good adherence to antihypertensive treatment involves a lesser degree of morbidity and mortality (HR 0.62 (0.40–0)) (Mazzaglia et al. 2009). Deficiency in compliance has an impact in most of cases in an increase in costs. These are generated due to an increase in hospitalizations and visits to the outpatient centers and emergency departments as well as changes in doses and prescriptions and more invasive diagnostic tests required (Hughes et al. 2001). Only in the United States, approximately 125,000 deaths per year

and 33–69 % of the hospital admissions are related to the lack of adherence to treatment, with an estimated total cost of 100 billion dollars annually: 25 billion corresponded to admissions and 70 billion to loss of productivity and premature death (Osterberg and Blaschke 2005; Ho et al. 2006; Dezii 2000; McCarthy 1998; Berg et al. 1993).

Patients with cardiovascular disease that fail to comply with their treatment regimen, have an 80 % increase in the risk of death in the first 120 days after an acute myocardial infarction (Newby et al. 2006). Non adherence to medication increases the risk of death from stroke in patients with hypertension (OR 3.81 (2.35; 3.20)) (Mayor 2013). Another study has shown that patients with diabetes, hypertension, high cholesterol, and heart failure, had higher hospitalization rates if they were low adherent (13 % vs 30 % for diabetics; 19 % vs. 28 % in hypertension) (New England Healthcare 2009). On the other side, there is a study pointing out a possible overestimation of the effect of poor compliance on the final outcomes (LaFleur et al. 2011).

3 Concept of Compliance

We can define ***compliance*** as the degree to which the behavior of the patient, in terms of medication, a diet or lifestyle changes, meets up clinical prescription or medical advice. Since compliance implies somehow blaming the patient, other terms have been used. As an example, ***adherence*** is defined as the capacity and willingness to comply with a prescribed therapeutic regimen (Sackett and Haynes 1976; Inkster et al. 2006). It is important to distinguish, as Haynes highlights (Haynes et al. 2008) between adherence and concordance in treatments. **Adherence** is the degree in which a patient meets the prescription ordered by his doctor, but sometimes this can have a guilty connotation. The **concordance** would be the degree of agreement on the treatment achieved by the patient and the physician. Three prerequisites are required in order that the patient has a good adhesion to treatment: it must be acceptable, understandable and personally manageable (James et al. 2016).

The Spanish Society of Hypertension Working Group on Compliance defines compliance as the extent that the patient assumes the rules or advices given by the physician or health professional, both from the point of view of lifestyle or the pharmacological treatment recommended. It shows the degree of overlap between the guidance given by the professional and the fulfillment by the patient after a fully reasoned decision (Márquez Contreras et al. 1998).

4 Types of Non-compliance

Non-compliance is a dynamic concept that may affect all phases of the clinical process from the first contact with the doctor until the end of the treatment. There is consensus in the literature that patients taking at least 80 % of the tablets are considered compliant.

On the basis of the Medication Event Monitoring System (MEMS) several patterns of non-compliance have been described (Márquez 2008; Márquez et al. 2012):

Compliers

- Absolute complier: person who takes quite the 100 % of medication
- Masked complier: person who takes more than 80 % of medication
- Sporadic failure: Non compliance with the treatment one to six times a month
- Over complier: person who takes more than 100 % of medication.

Non Complier

- Absolute breach: person who takes less than 50 % of medication.
- Partial non-compliance: individuals taking between 50 and 80 %.

- Medication abandonment: patients definitely stop taking their medication.

Others Patterns

- Drug holidays: individuals who do not take their medication for three days.
- Predicted non-compliance: repetitive non adherence at certain times.
- White coat effect: non compliers individuals that take their medications the days before an appointment.
- Time table non-compliance: do not take the medication at the scheduled hours medication hours.
- Mixed non-compliers: coexistence of two or more associated patterns.

With the advent of integrated electronic prescribing and dispensing data they can be classified in (Tamblyn et al. 2014; Fischer et al. 2010):

Primary non adherence: it was defined as failing to fill a new incident prescription.

Persistence or secondary non adherence: the patient stop taking medications soon after filling the first prescription

5 Factors Involved

The general factors involved in adherence of the treatments can be classified in (Rosenson et al. 2016):

- Cognitive losses cause forgetfulness of dose or loss of ability to understand the impact of treatments
- Psychopathology: the depression, anxiety or high levels of hostility may affect compliance
- Functional illiteracy affects to the compression of the treatments.
- The interaction with the professionals of health may improve compliance using non-technical words and involving the patients in the decisions.
- The lost in the clinical follow-up of patients with chronic diseases affects the adhesion and the final objectives of the treatment

The most frequent barriers are related to the characteristics **of the patient and disease** (simple forgetfulness, ignorance of the chronic disease condition, retirement (Kivimäki et al. 2013), poor social, health or family support and personal decision of the patient to give up treatment). Some are also dependent on the **characteristics of the treatment** (side effects, long-term therapies, difficult to understand or to take, inadequate communication, price) (Baroletti and Dell'Orfano 2010). Although age is not a risk factor per se, there are several studies that suggest that non-adherence, intentional or not, is a problem in aged patients. This is due, in part, to the lack of understanding of the schemes available and the forgetfulness, favored by the high proportion of elderly people who live alone, the impairment of cognitive function, the prevalence of co-morbidities and the polimedication (Horne et al. 2005; Wang et al. 2014)

An interesting systematic review with qualitative research methodology concludes that patients with hypertension link together stress and the presence of symptoms (Marshall et al. 2012). This perception justifies treatment abandonment when they perceive less stress or less symptoms. Sometimes they stop treatment if they are afraid of side effects or a possible addiction to treatment. No ethnic or countries differences were detected. A factor who influence in the adherence to treatment is the **patient-physician relationship.** It is important to know the beliefs and expectations of the patient, as well as the socio-familial support. It is the family in many cases that acts as a reminder of the treatment and can promote a change of conduct. The success of treatment depends on both: therapist and patient. For a solid grip, the doctor requires technics and tools in communication skills (Sanson-Fisher and Clover 1995).

6 Prevalence of Treatment Adherence

According to a systematic reviews, the prevalence of non-compliance with HTA treatment in the world is, at average, 30 % and probably this is one of the main causes of the lack of control of hypertension (Tamblyn et al. 2014; Cramer et al. 2008). The therapeutic compliance prevalence ranges between 40 and 90 % according to the method used to measure, the disease and the population studied. In this sense, Choo and collaborators (Choo et al. 1999) they assessed the validity of self-reported compliance, pharmacy records and counting tablets as measures of antihypertensive drugs compliance against the MEMS standard. Hansen (Hansen et al. 2009) and Horne (Horne et al. 2010) also compared different methods of measurement of compliance, with figures between 80 and 90 %. Other authors that also used MEMS system as control, found a compliance rate around 80 % (Zeller et al. 2007; Santschi et al. 2008). In a series that evaluated the compliance evolution in 3553 patients during 20 years, an increase in compliance was detected, although the final rate was 67.47 % (Márquez et al. 2006). This contrasts with a study performed in non-industrialized countries where the average compliance was 40 % even after using the same method (Qureshi et al. 2007). Besides, Schoenthaler found a compliance rate of 56 % in African Americans (Schoenthaler and Ogedegbe 2008).

The different studies available show conflicting results. It is difficult to obtain significant relations with the compliance variable, as long as this variables depends largely on individual factors that are difficult to assess. Some works highlight that the presence of other chronic diseases associated to high blood pressure adversely affect taking medication: multiple drugs are required for the control of the diseases. So, patients with high cardiovascular risk sometimes use 4 or more drugs to control several diseases that can cause undesired side effects and trigger low adhesion (Morris et al. 2006; Chapman et al. 2005; Gregorie et al. 2006; Sicras et al. 2006). DiMateo and collaborators published a meta-analysis of studies published over nearly six decades. They concluded that patients with severe disease and a poor state of health should be identified as of great risk of being non-compliant with treatment (DiMatteo et al. 2007).

To achieve the therapeutic objectives in hypertension, health professional must consider that each patient has priorities in health and that each person has an **"acceptable therapeutic load"**; i.e. the maximum number of medications that are considered reasonable to take every day. This number varies from person to person and the physician needs to know it in order to plan treatment (van Duijn et al. 2011). Some authors suggest that non adherence to treatment is induced by the health system. They propose a **"minimally disruptive medicine"** (May et al. 2009; Dabrh et al. 2015) with 4 principles: determine the load weight which is acceptable for each patient, enhance coordination in clinical practice with an holistic vision, increase the knowledge of the co-morbidity in clinical practice, and prioritize the patient autonomy and its perspective.

7 Methods to Measure Adherence

It is necessary to know the degree of adherence both to make decisions on the follow-up of the patient as to assess the outcome of clinical trials. There are several methods to measure compliance and are classified into direct and indirect (Márquez 2008; MacFadyen and Struthers 1997). In general, the former tend to be more sensitive and specific, but less acceptable to the more invasive.

Direct methods measure the amount of drug, metabolites, or markers found in some body fluids. Methods are more objective and specific but expensive and inaccessible in primary care. They are also inefficient for short half-life drugs. The use of liquid chromatography-mass spectrometry analysis for antihypertensive drugs in urine analysis can detect low compliance in patients with

Table 2 Indirect methods for evaluating compliance of hypertension

Method		Advantages	Disadvantages	Validation[a]			
				S	S	PPV	NPV
Based on the table count	Simple count of tablets	Objective, quantifiable	It takes time. It does not detect the drug intake. High price	Gold standard in research studies			
	Medication Event Monitoring System (MEMS)						
Based on the clinical interview	Haynes-Sackett test	Simple, quick. Useful in clinical practice	It overestimates the adhesion	0.33	0.93	0.73	0.69
	Test of Morysky			0.49	0.68	0.48	0.68
Other methods	Professional judgment	Simple, fast	Vague	0.28	0.78	0.44	0.64
	Assistance to appointments	Simple	It also depends on the health care organization	0.71	0.83	0.43	0.65
	Improvement of disease	Simple, easy to apply	Interference from other factors such as co-morbidities	0.53	0.62	0.46	0.68
	Knowledge of disease	Simple	Dependent on the level of culture of the patient	0.82	0.41	0.46	0.79

[a]From Márquez (2008)
S sensitivity, *S* specificity, *PPV* positive predictive value, *NPV* negative predictive value

refractory hypertension (Jung et al. 2013; Tomaszewski et al. 2014).

Indirect methods are simple and economic, useful in the clinic, but their disadvantage is that they are not objective and tend to overestimate the adherence to the treatment. They are based on the quantification of the number of tablets or on clinical interviews. These are the most widely used (Table 2).

7.1 Clinical Interview-Based Methods Most Commonly Used Are

7.1.1 Haynes-Sackett or Self-Reported Compliance Test (Sackett et al. 1975)

It consists of two parts. The first part avoids a direct question, and in a friendly environment, the following sentence is inserted:

> "the majority of patients have difficulty taking their tablets, do you have difficulty in taking all your own?".

This approach eases the identification of poor adhesion. If the answer is Yes, the patient is non-compliant, and he will be questioned on the tablets taken in the last month. The authors considered complier a patient whose percentage of self-reported compliance is between 80 and 110 % (Stephenson et al. 1993).

7.1.2 Morinsky-Green Test (Morisky Medication Adherence Scale-4 Items, MMAS-4) (Morisky et al. 1986)

It is a questionnaire that can help the professional to identify the poor adherence to antihypertensive treatment. This method has been validated for several chronic diseases, although it was initially developed by Morinsky, Green and Levine to assess compliance with medication in patients with arterial hypertension. A patient is considered a good complier if answers correctly to 4 questions conducted, interspersed in a cordial way, during a conversation about her illness:

1. Do you ever forget to take the drugs for your illness?;
2. Do you take your medication at the indicated hours?;
3. Do you stop taking your medication when you feel well?

4. If you ever feel ill, do you quit your treatment?

There is a **version of the questionnaire with 8 items (MMAS-8)** (Morisky et al. 2008; Gallagher et al. 2015) It also includes questions on the reasons for non-adherence. It is useful to propose improvement strategies with the patient. The authors determinate low adhesion if the patient has less than 6 correct answers, average adhesion between 6 and 8 and high adhesion if 8 questions are correct.

1. Do you sometimes forget your high blood pressure pills?
2. Over the last two weeks, were there any days that you did not take your high blood pressure medicine?
3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?
4. Do you sometimes forget to bring along your medication when you travel or leave home?
5. Did you take your hight blood pressure medicine yesterday?
6. Do you sometimes stop taking your medicine when you feel your blood pressure is under control?
7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your blood pressure treatment plan?
8. How often do you have difficulty remenbering to take all your blood pressure medication?

7.2 Methods Based on Tablet Quantification

7.2.1 Medication Event Monitoring System (MEMS)

They use the **Medication Event Monitoring System (MEMS).** These are monitoring systems based on a computerized registration. A microchip placed on the top of the container records the date and the time in which the container is opened. This method is often regarded as the gold standard to measure the adhesion. However, it only detects the opening, not the drug intake, it is not useful in routine clinical practice and it is expensive (Choo et al. 1999; Rosen et al. 2004).

7.2.2 Simple Tablets Count

It is a simple and objective method that compares the number of pills remaining in the container, taking into account the prescribed and the time elapsed between the prescription and the moment when they are measured. A patient is considered good compliant when has consumed 80–100 % of the prescribed tablets. This method tends to overestimate compliance when the patient assumes that it is controlled or if the drug is consumed by another member of the family (Bond and Hussar 1991).

7.3 Additional Compliance Estimations (Márquez et al. 2006)

- There are other practical measures, although less used as the ***Batalla test***. This test analyze the degree of ***knowledge that the patient has of his illness,*** assuming that the greater patient awareness, the more compliant he will be.
- ***The health professional judgement***: based on the opinion of the doctor or the nurse on the patient. The compliance is considered according to the health professional criteria.
- Th***e assistance to scheduled appointments:*** if the patient does not attend the appointments, he is considered a bad compliant.
- ***Method based on the improvement of the treated disease***: If hypertension is controlled that would indicate us that the patient is a good complier.
- ***Method based on the medication collection*:** It is based on the quantification of the medication withdrawn from the pharmacy. The computer records (e-prescribing) report if the patient goes to renew prescriptions on time.

Usually, patients tend to overestimate their adherence to medication, and unless a patient fails to respond to therapy, it is difficult detect a

low compliance. If the patient affirms he is a good complier in the clinical interview and we are suspecting non-compliance, we will have to check medication collection in the chemist records and count the tablets used either in the clinic or at home. The count can be masked indicating the patient that we are simultaneously evaluation the expiration. This is the method of choice for general research, but if you want to know the pattern of non-compliance the count will be used through MEMS.

8 Improvement Strategies

8.1 Doctor-Patient Relationship and Treatment Compliance

The style of communication preferred to improve the performance of treatments is a patient-centered style. Thus, it is useful to ask how the patient understands his illness ("what do you known about hypertension?, Which organs can be affected? Do you think that you can control it?). In this way we explore their attitudes and expectations. Patients who understand the personal consequences of their risk factors can manage better the information. In a structured way and to advance in the knowledge of the beliefs of the patient on the arterial hypertension we can use questionnaires based on the Self-Regulatory Model (Ross et al. 2004).

Patients often express their fears to take several drugs or become dependent on them (eg: "When I have to take so many medications, I feel old" "When my labs are normal, I can quit treatment"). Therefore we should ask about the compliance in a non-punitive manner and in the context of the particular values of the patients (eg: "it's hard to take so many pills, How many times does it happen to you?"). Clinicians must have a long-term perspective and see failures as a learning tool.

The communication strategy to improve adherence should include: the use of non-technical language adapted to the cultural level of each person, personal experience in other drug use, discuss with the patient expectations of benefit and adverse effects, modify ideas and misconceptions, incorporate the preferences of the patient in the treatment plan, give written instructions in a clear and simple way, recommend pill boxes to organize the medication, involve family members, discuss the need to keep the medication despite feeling well. Try to improve the adhesion with a confrontational style with the patient is rarely useful (James et al. 2016).

8.1.1 Shared Decision Making (SDM)

Involving the patient in decision-making and a collaborative integration is beneficial in the management of chronic diseases. We have studies in hypertensive patients where shared decision-making strategy improves therapeutic adherence and control of hypertension. There are studies with SDM in several health care professionals such as physicians, pharmacists, nurses and dieticians. This strategy also showed benefit in poorly controlled hypertension patients with computer-based decision-making tools (van Duijn et al. 2011; Houle et al. 2014; Buhse et al. 2015; Tinsel et al. 2013; Buchholz et al. 2012; Abel and Barksdale 2012; Paasche-Orlow 2011; Roshanov et al. 2011).

8.1.2 Motivational Interview

The motivational interview technics based on the stages of change model of Prochaska and Di Clemente demonstrated some benefit in lifestyle and adherence to treatments (Miller and Rollnick 2013). There are three systematic reviews of clinical trials performed with this technique that presents a statistically significant improvement over conventional interventions with an estimated OR 1.55 (1.40; 1.71). The benefit is particularly promising in weight loss, alcohol and tobacco consumption, sedentary life style self-monitoring and treatment adherence (Lundahl et al. 2013). O'Halloran meta-analysis was performed with studies on people with chronic diseases (O'Halloran et al. 2014). VanBuskirk published another systematic review on primary care population with good results for weight loss and blood pressure. The motivational interview seems to be useful in clinical settings

and one single session can improve the willingness to change and an action for health goals for behavior changes (VanBuskirk and Wetherell 2014).

The benefit of the motivational interview has been validated in different healthcare professionals: physicians, nurses and pharmaceuticals (Stewart et al. 2014; Klamerus et al. 2014; Ma et al. 2014; Drevenhorn et al. 2012). The health professional must know in which stage of change is the patient for lifestyles or taking medication changes, as long as the management strategy is different in each stage. The stage of the change of the patient can be classified as shown below:

- Not thinking about it at all (pre-contemplation stage)
- Thinking about it (contemplation stage)
- Ready to start planning (preparation stage)
- Ready to implement it (Action stage)
- Already making the change (Maintenance stage)

8.2 Factors Associated with Disease and Treatment

We have three Cochrane reviews on different intervention studies to improve compliance and control of hypertension. The different interventions can be classified as:

8.2.1 Health Education to Patients and Professionals

Trials of educational interventions to patients or professionals in general are not related to significant reductions in blood pressure. Clinical studies show that the effects of reducing the BP with changes in lifestyle can be equivalent to monotherapy with drug but the main drawback is the low level of adhesion as time passes (Elmer et al. 2006). There is a consensus that when patients get the information material available in press, pharmacies, medical clinics or other public places offices, it can have a favorable effect on information and motivation of the persons concerned (Guthrie et al. 2007).

A Cochrane review (Glynn et al. 2010) including 20 randomized clinical trials (RCTs) educational interventions directed to the patient was performed. The combination of the results of all RCTs produced mixed results. The mean difference in systolic blood pressure (SBP) and diastolic (DBP) was not statistically significant. With respect on the blood pressure control, there was a trend towards an improvement in the control (Odds Ratio 0.83; 95 % CI: 0.75–0.91). In the same systematic review, ten RCT with educational interventions directed to the health professional were analyzed. These interventions were not associated with a significant decrease in SBP and DBP, nor with a significant increase in the blood pressure control.

The tendency to minimize the high figures of the BP by the physician is denominated therapeutic inertia. Medical training programs significantly reduce therapeutic inertia therapeutic although with fewer benefits than expected (Redon et al. 2010; Luders et al. 2010).

8.2.2 Reminder Systems

Glynn reviewed eight RCTs with interventions aimed at reminding the patient appointments and encourage self-monitoring of the efficacy of the treatment. The systems were diverse: from postcards, phone reminder notices by text messages to computer feedbacks. Pooled results were associated with an improvement during follow-up (Odds Ratio of losses to follow up 0.4; 95 % CI: 0.3–0.5). However, we have the study could not determine which reminder system was the most effective (Glynn et al. 2010).

The impact of information and communication technologies in general, and particularly the computerized decision support systems, is discussed in detail in the health security report published by the European Commission in 2007. The report argues that these systems can prevent medical errors and adverse events, promote the participation of the patient with an advantage due to cooperation and adherence (OECD www.oecd.org; Russell et al. 2009).

New technologies, allow that more patients can be controlled, the contacts may be more frequent, with a greater chance to address their concerns, adapt treatment and ultimately improve the adhesion. However, it is important to note that these new care delivery models do not represent a substitute for visits to the physician's office. Rather, they offer support for the strategy of establishing a good relationship between the patient and the health care professionals. Studies using communication technologies have demonstrated that there are many ways to communicate with patients, with the theoretical advantage of appropriate adjustment and effective care plans.

8.2.3 Treatment Simplification

Adherence to treatment can also be improved through treatment simplification (Claxton et al. 2001) A Cochrane review reviewed nine RCTs on treatment simplification (Schroeder et al. 2004). The simplified dosing regimens improved compliance in seven of the nine studies, with an improvement in the fulfillment that varied from 8 to 19.6 %. Studies that were made using MEMS showed improvement in compliance when one dose a day was used instead of two. The type of antihypertensive drug is related with compliance. Thus, in the meta-analysis published by Kronish et al., the highest adhesion was found with angiotensin II-receptor blokers and angiotensine-converting enzyme inhibitors, the lowest with beta blockers and diuretics (Kronish et al. 2011).

It is more likely to achieve the goals of blood pressure control in patients with higher blood pressure values with combination therapy. We have recent studies that have shown that patients receiving fixed-dose combination therapy have a lower abandonment rate (Corrao et al. 2010). The use of polypills (fixed-dose drug combinations) greatly simplifies the number and doses of drugs and is an interesting field to improve adhesion. Polypills lowers cost of production and distribution, improve accessibility to treatment especially in middle and low income countries (Muntner et al. 2011).

8.2.4 Pharmacists and Nurses Care

Several studies show a greater reduction of the BP in groups with multidisciplinary care teams, when compared with the conventional approach. Nurses and pharmacists either within a clinic or in the community are beneficial in reducing the BP. The participation of nurses and pharmacists in the management of hypertension has obtained benefit when they are involved in the patient education, advice and evaluation of adherence to the treatment. The contribution of nurses may be particularly important for the implementation of the changes of life style (Carter et al. 2009; Walsh et al. 2006). A recent study confirms the positive effect of pharmacists interventions on compliance (Hedegaard et al. 2015).

The systematic review conducted by Glynn in 2010 brought together 12 RCTs with pharmacists or nurses care. Pooled results show that the mean for the SBP difference was from − 13 to 0 mmHg. And the DBP was from − 8 to 0 mmHg. With respect to the degree of blood pressure control, the results were not significant (odds ratio ranged from 0.1 to 0.9). The authors of the review conclude that these health professionals care can be an excellent way to provide assistance, since the majority of RCTs are associated with better control of blood pressure (Glynn et al. 2010).

8.2.5 Self-Monitoring

There are 18 RCTs evaluating the effect of self-monitoring of the AP by the patient that wer analyzed in a systematic review (Glynn et al. 2010). The pooled data showed that self-monitoring was associated with a significant reduction in the mean SBP: − 2.5 mmHg (95 % CI: − 3.7 to − 1.3 mmHg). The mean DBP showed a more modest decline of − 1.8 mmHg (95 % CI: − 2.4 to − 1.2 mmHg). With regard to the control of blood pressure, there was no significant improvement (Odds Ratio 0.97; 95 % CI: 0.81–1.16). In this line, Uhlig concluded that self-monitoring of blood pressure drops blood pressure compared to usual care, but the effect beyond the 12 months is

uncertain in a meta-analysis published in 2013 (Uhlig et al. 2013). Tele-monitoring at home proved to be useful in patients with hypertension. Several studies have confirmed that the electronic transmission of the self-BP monitoring favors better adhesion to the regime of treatment and is a more effective control of hypertension (McManus et al. 2010; Morak et al. 2012; Shea and Chamoff 2012; Parati et al. 2009).

8.2.6 Interventions to Improve the Provision of Care Services

The systematic review published by Glynn et al. in 2010 (Glynn et al. 2010) analyzed 9 RCTs with organizational interventions to improve care for hypertensive patients. Pooling of results from the individual RCTs produced mixed results. The largest clinical trial, the Hypertension Detection and follow-up Program (HDFP) (The effect of treatment on mortality in mild hypertension results of the Hypertension Detection and Follow up Program 1982) that included around 10.940 people, obtained appreciable reductions both in sBP and dBP. After a five year follow-up period, these reductions in blood pressure were associated with a 28.6 % significant reduction in mortality from all causes. The organizational measures of this study consisted of a free of charge care, active follow-up visits on a regular basis and a steps use of antihypertensive drug therapy.

8.3 Factors Related to the Health System

8.3.1 Costs

Recently, an increase in compliance was found in those patients taking generic drugs when compared with those taking registered trademark drugs. Besides, a reduction in the vascular events was also founds (Gragne et al. 2014). These data were obtained in populations with low incomes, so it cannot be extrapolated to other populations where the drug cost may be less important for adhesion. Other studies confirm that the price of prescription drugs influences the therapeutic non-compliance. An example is a study that showed that patients who had had a cardiac event and subsequently did not have to pay a high price for their medication, presented a better performance and were less likely to have recurrences of the heart disease (Susan 2015; Chourdhy et al. 2011).

Sometimes, when the price of drugs is high, some patients skipped doses or do not continue with the prescription when it finishes. This makes the physicians that the prescribed medication was not enough with a subsequent unnecessary dose increase. Health care co-payment policies can lead to the patient to use fewer medicines or to choose the cheapest. Although this can avoid using unnecessary medicines, they can also cause harm when treatments for the control of chronic diseases are abandoned (Baroletti and Dell'Orfano 2010; Luiza et al. 2015) The minimum dose required should be prescribed using generics, and informing the patient about the most cheap available drugs. The use of cheaper medication tries to reduce costs and prevent barriers in the access to medication (Kaplan et al. 2016). Today, we have generic drugs and cheap options in all classes of antihypertensive medication (Choudhry et al. 2016).

8.3.2 Social Support and Self-Help Groups

There are interesting studies of community-based intervention on cardiovascular problems among adult assistance programs similar to other self-help organizations. They do not require the active presence of doctors or nurses and focuses on the empowerment of the patient and the formation of "expert patients" and community agents. Their results indicate an improvement in adhesion and achievement of the objectives of cardiovascular health in chronic diseases (Fuster et al. 2011; Vedanthan et al. 2014).

Interventions have also been developed in order to organize a network of social support in relation to physical activity, sodium intake, weight control or reduction of alcohol consumption. As an example, the project "walking with a friend to health" intends to include the community in the prevention measures and hypertension

control. In this way, it obtains support for early intervention, prevention, and treatment of high blood pressure through the organizations of patients and relatives. So, the relatives of the patients and their support network become supporters of the treatment plan (Fishman 1995).

The incorporation of the family, the community, and organizations is a key factor for success in the improvement of adhesion. Living alone is a major cause of non-compliance. Accordingly, a poor perception of social support received by the patient is linked to reduced physical activity and poor adherence to the diet. Several research studies have concluded that social support improves adherence to treatment in hypertensive patients. In this way, patients who have wide social support networks or those who are married or in couple indeed, have better adherence. Social support is also essential when long-term treatment are planned that require continuous actions by the patient (DiMatteo 2004; Oegdegbe et al. 2004; Bosworth 2010). It is not only necessary an increase in family support. Research has shown that participation in patient groups is an effective strategy of motivation (Sherbourne et al. 1992; Coull et al. 2004). There is substantial evidence that support between pairs of patients can improve adherence to therapy and, at the same time, reduces the amount of time spent by the health care professionals to care for chronic diseases (WHO 2004).

8.4 Multiple Interventions

As the therapeutic non-compliance is complex issue that is influenced by variety of factors it seems logical to design interventions with multiple strategies to try to improve it. In this sense, there are studies with multiple interventions such as: reminders, pill containers, self-monitoring of blood pressure, treatment simplification, pharmacists or nurses support, family interventions, or the provision of educational material to the patient; that achieved improvements in compliance (Marquez et al. 2006). In this sense, the COM99 study (Pladevall et al. 2010) confirmed that combination of strategies is always more effective than a single one.

In another systematic review on adherence Haynes (Haynes et al. 2008) and his collaborators analyzed 70 RCTs and found 83 types of different interventions. They conclude that multifactorial interventions are most effective in modifying the adherence to long-term therapies. These studies included combinations of information, reminders, self-monitoring, reinforcement, counseling, family therapy, psychological therapy, crisis intervention, telephone follow-up and support care. Due to the heterogeneity of the studies they could not evaluate the individual effect of each strategy on the control of hypertension, or which combination was the most effective. With respect to the quantification of the effect of interventions the authors are cautious and conclude that even the most effective interventions did not result in great improvements in adherence and treatment outcomes. Marquez and colleagues refer that these interventions can control BP in two out of three patients with high cardiovascular risk and a poor BP control and the number needed to treat to prevent one patient with poor hypertension control is five (Márquez et al. 2012). In Table 3 we present a summary of the practical strategies to improve adherence.

9 Recommendations of the Clinical Practice Guidelines

9.1 European Society of Hypertension (ESH/ESC) Guideline

European society of hypertension (ESH/ESC) guideline (ESH/ESC 2013) give great relevance to the low level of compliance observed, especially in elderly and poor patients, due to its influence in prognosis and healthcare costs. They emphasize that low adherence to treatment is the most important reason for poor control of the BP and that this fact has been fully documented (Lee et al. 2006; Gale et al. 2011;

Table 3 Interventions to improve adherence: practical strategies

Type of intervention	
Physician related	Before you increase the medication think about compliance. Enter medication in a step ahead fashion. Use the minimum effective dose to avoid side effects. Avoid therapeutic inertia
Relationship doctor – patient	Explain the indication of each pill and its side effects. Report of the blood pressure values. Ask for adherence with a non-confrontational style. Use the motivational interview techniques: in the event of poor compliance, identify in which stage of change the patient is
	Involve the patient in decision-making
	Note the mood of the patient and its cognitive function
Treatment simplification	Use the minimum number of drugs and minimum number of possible dose
	Use fixed-dose combinations
	Recommend the use of pill boxes and organizers for medication
	Associate taking medication with a routine of the patient. Provide written information
Reminders	Keep the contact with the patient. Schedule an annual review and share with him the clinical situation. Use reminders: telephone, computer or postal. Contact patients that are not attending the clinic. Check the collection of medication in the pharmacy records
Self-monitoring of BP	Recommend self-monitoring blood pressure
Cost of drugs	Use cheap and generic drugs
Collaboration with other professionals	Promote the control of hypertension by pharmacists and nurses.
	Incorporate organizational improvements in the care of hypertensive patients
Social support	Involve family members in the treatment
	Recommend self-help groups and patient forums.
Multiple interventions	Use at least three strategies together

Shanti and Maribel 2003; Krousel-Wood et al. 2011; Corrao et al. 2011; Mazzaglia et al. 2009).

With regard to **the identification of low adherence to treatment** in clinical practice they point out that there are difficulties because the information provided by the patient can be misleading and methods for objectively measuring the adherence to treatment have little application in daily medicine.

The guidelines make a series of recommendations to promote adherence to medication, with **the simplification of the drug regimen** as the isolated more effective recommendation. As in the previous guidelines, the 2013 ESH/ESC guidelines favor the use of combinations of two antihypertensive doses fixed in a single pill, since reducing the number of pills taken daily improves adhesion.

The guideline stresses the relevance of **reporting BP values**, even in visits that are not related to hypertension. They also recommended the use of **self- monitoring blood pressure** at home (Parati et al. 2010).

The European guidelines insist in avoiding the **therapeutic physician inertia** (Banegas et al. 2004), attitude that tends to minimize the relevance of high blood pressure levels. They point out that if high AP is detected, the reason must be searched. The most common causes are poor adherence to the prescribed regimen, the persistence of a white coat effect and the occasional or regular consumption of substances that increase BP.

On the other hand, they recommend **multifactorial interventions** and to enhance **the role of nurses** as a possible strategy to improve adherence to treatment (Berra et al. 2011). The guideline points out that multidisciplinary cardiovascular prevention programs co-ordinated by a professional nursing improve the control of risk factors, susceptibility to physical activity and adherence to treatment compared with usual care. Besides, it also improves

the perception of the patient's health, especially in secondary prevention.

The **multidisciplinary team** -based care (Machado et al. 2007) with the participation of pharmacists and nurses can improve adhesion and reduce the BP and, thus, it is also recommended by the European guideline.

The ESH/ECH published its recommendations on how to organize the work team for the management of hypertension in centers of excellence (Stergiou et al. 2010). It recommends a close contact with the patient and the use of telemedicine to improve compliance with treatments, as well as the incorporation of other models for care continuity.

9.2 The NICE Guidelines

The NICE guidelines (2011) in his chapter on education and adherence in hypertension recommends

- Provide appropriate guidance and materials about the benefits of drugs and the unwanted side effects sometimes experienced in order to help people make informed choices
- People vary in their attitudes to their hypertension and their experience of treatment. It may be helpful to provide details of patient organizations that provide useful forums to share views and information
- Provide an annual review of care to monitor blood pressure, provide people with support and discuss their lifestyle, symptoms and medication
- Because evidence supporting interventions to increase adherence is inconclusive, only use interventions to overcome practical problems associated with non-adherence if a specific need is identified. Target the intervention to the need. Interventions might include:
  - suggesting that patients record their medicine-taking
  - encouraging patients to monitor their condition
  - simplifying the dosing regimen
  - using alternative packaging for the medicine
  - using a multi-compartment medicines system

9.3 The Recommendations of the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

The recommendations of the Panel Members Appointed to the Eighth Joint National Committee (JNC 8) (James et al. 2014) choose an individualized treatment strategy. This strategy should be adapted on the basis of the particular circumstances of the doctor, the preferences of the patient and the tolerance to the drug. Within each strategy, physicians should regularly assess BP, foster evidence-based interventions in lifestyle and adhesion. The Panel recognizes the importance of treatment adherence and medication costs but experts think that these issues are beyond the scope of their recommendations

9.4 Report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents Developed in Collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension

An important set of scientific societies (Aronow 2011) have made specific recommendations for elderly hypertensive patients. They conclude that "elderly patients who are taking more than

6 medications present a lower adherence to treatment. So clinicians must take account of polypharmacy and potential pharmacological interactions, as causes of low adherence to treatment".

10 Conclusions

1. The lack of adherence is very prevalent in hypertension with a multifactorial etiology.

2. Elderly patients, those with several co-morbidities, social isolation, low incomes or with depression are the most vulnerable to this problem.
3. There is no an ideal method to quantify the adherence to the treatment. Indirect methods are recommended in clinical practice.
4. Any intervention strategy should be based in not blaming the patient and a collaborative approach. It is recommended to involve the patient in decision-making. The clinical interview style must be patient-centered including motivational techniques.
5. The strategies that demonstrated greater effectiveness in hypertension treatment compliance were: treatment simplification, systems appointment reminders, self-monitoring of blood pressure, organizational improvements and nurse and pharmacists care.
6. Combined interventions are recommended instead of isolated interventions.

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