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REVIEW

ADHERENCE TO ANTIHYPERTENSIVE TREATMENT IN COGNITIVELY IMPAIRED AGED: A SYSTEMATIC REVIEW

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ABSTRACT

Objective: to verify the influence of cognitive impairment on adherence to antihypertensive treatment in the aged. Method: systematic review, with the inclusion of original articles, available in full, in Portuguese, English and Spanish, published between the years 2007 and 2021. The search was made in SCIELO, PUBMED, LILACS and MEDLINE, with the following descriptors: "Cognitive Dysfunction"; "Medication Adherence"; "Hypertension"; "Aged". Results: of the 216 studies found, five were selected. Four showed a negative relationship between cognitive impairment and adherence of the aged to antihypertensive treatment. It was evidenced that aged with cognitive impairment were more likely to have inadequate blood pressure control. Conclusion: it is observed that cognitive impairment is an important risk factor for poor adherence to treatment in hypertensive aged. Early detection becomes essential, aiming to adapt care to the cognitive conditions of the aged and optimize medication management to achieve adequate control of blood pressure levels.

DESCRIPTORS: Cognitive Dysfunction; Medication Adherence; Hypertension; Aged; Systematic Review.

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INTRODUCTION

The fast population aging process in Brazil today represents a major challenge to the public health system[1-3]. It is estimated that the world population of aged, which was 901 million in 2015, is expected to increase to 1.4 billion in 2030 and to 2.1 billion in 2050. Although a substantial increase in the number of aged people is predicted in all countries, this growth is expected to be considerably higher in developing regions[4]. For Brazil, whose aged population in 2014 represented 13.7% of the general population, this percentage is projected to increase to 18.8% in 2030 and to 29.3% in 2050[4-5].

Simultaneously to the demographic transition, there are changes in the epidemiological profile of the population, with relevant alterations in the morbidity and mortality picture, which is now characterized by the presence of Chronic Noncommunicable Conditions, currently responsible for more than 70% of deaths in Brazil, requiring constant monitoring and permanent care, as well as continuous use of medication and periodic exams[6-8].

Systemic Arterial Hypertension (SAH) is the most common chronic disease among the aged. Its prevalence progressively increases with aging and because it is an asymptomatic condition, patients neglect treatment, which can lead to cardiovascular complications[9-10]. It is also considered the main modifiable risk factor in the geriatric population[11].

The control of SAH is directly related to the level of adherence to treatment, defined as the degree to which a person's behavior, represented by taking medications, following diet, and making lifestyle changes, corresponds, and agrees with the recommendations of the physician or other health care professional[12].

The term adherence expresses the voluntary and active participation of the user in the development and adjustment of the care plan[13]. It is a desirable and expected behavior for people with chronic conditions[12]. However, national, and international studies have shown that the levels of adherence to hypertension treatment are still low and range from 8.7% to 59.6%, according to the population studied and the form of assessment[14].

Non-adherence to drug treatment is one of the main causes of treatment failure, irrational use of drugs, and aggravation of the disease process, which can negatively affect the patient's clinical evolution and bring several consequences, such as low therapeutic results and preventable costs to the health system[15].

Several factors may contribute to non-adherence to treatment, highlighting among them the difficulties in accessing health services and medications, sociodemographic factors, problems with complex therapeutic regimes, adverse effects, insufficient guidance to understand and follow the prescription, inadequate doctor-patient relationship, or even inability to afford treatment costs[16-17]. Some studies point out that cognitive deficit is another relevant risk factor associated with non-adherence to antihypertensive treatment in the aged[18-19].

For the study of this cognitive deficit, several terms have been proposed, including Mild Cognitive Impairment (MCI), Incipient Dementia, Non-Dementia Cognitive Impairment, Dementia Prodromes, Pre-dementia, among others, with minor differences in their definition criteria. Despite the differences, all concepts refer to individuals who are not demented, with preserved or minimally impaired functional capacity, but who have measurable cognitive deficits and a high risk of developing dementia. The most widely used term to characterize this "gray zone" between normality and early forms of dementia is Mild Cognitive Impairment[20].

Cognitive functions are not significantly affected in aging; global cognitive deficit can occur without, however, compromising the autonomy and independence of the aged. The impairment occurs basically in the executive functions, making it difficult to perform several

tasks simultaneously and slowing down the process of learning and retrieving information. Significant forgetfulness, therefore, is not part of the normal alterations of senescence[21].

Thus, the changes and deficits caused by significant losses in cognition can have direct consequences on the quality of life of the aged, and can lead to functional decline, with decreased ability to develop activities of daily living[22], which may interfere with the ability to understand and carry out the recommendations of the proposed therapeutic scheme, by the need for assistance for self-care.

Studies have not presented consistent results about the influence of cognitive impairment on adherence to antihypertensive treatment in the aged. For instance, a cohort study[23] found that the risk of non-adherence was higher in those with moderate cognitive impairment compared to those without cognitive impairment, like other studies[18,24]. However, other research[25] has shown that the aged with cognitive impairment adhered more to drug treatment.

Considering these aspects, this article aims to analyze the influence of cognitive impairment on adherence to antihypertensive treatment in the aged, based on the scientific literature.

Understanding the relationship between cognitive impairment and adherence to drug treatment in hypertensive aged people can support health care for health professionals, especially in Primary Care. Thus, they can improve efforts to promote interventions focused on prevention and directed to individual particularities and the specificities of the aged population, aiming to favor better blood pressure control.

METHOD

This is a systematic literature review, carried out according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[26]. The search for articles was conducted from March to May 2021, in the following databases: Scientific Electronic Library Online (SCIELO); US National Library of Medicine and the National Institutes Health (PUBMED); Latin American and Caribbean Literature on Health Sciences (LILACS) and Medical Literature Analysis and Retrieval System Online (MEDLINE). The following descriptors were used: "cognitive dysfunction"; "medication adherence"; "hypertension"; "aged", and their equivalents in English and Spanish, obtained from the Descriptors in Health Sciences (DeCS) and Medical Subject Headings (MeSH), used jointly, combining them through the Boolean operators "OR" and "AND" with different search strategies, according to the specific characteristics of each database.

To construct the research question, the PICO strategy was used, which stands for Patient, Intervention, Comparison and Outcomes (outcome)[27]. According to these components, the following terms were considered: aged and hypertension (for patient); cognitive dysfunction (for intervention); medication adherence (for outcome); the "C" element was not used, since the present study does not aim to compare different interventions.

The articles were initially selected based on the information contained in the titles and abstracts, and then read in full and evaluated according to the eligibility criteria. Duplicate articles were identified and excluded. In situations in which the title and abstract were not enlightening, the article was also read in its entirety to avoid the exclusion of important articles of interest to the objectives of this research.

Inclusion criteria were original articles, available in full, in Portuguese, English, and Spanish, published between 2007 and 2021, that addressed the relationship between

cognitive impairment and treatment adherence in aged (≥60 years) hypertensive patients without dementia. We excluded book chapters, dissertations, theses, letters to the editor, case or series reports, congress proceedings, reviews, editorials, articles without abstracts or with emphasis only on adherence.

To record the information obtained from each selected article, an instrument was used consisting of the following items: author, year, country, language, objectives, study design, sample size, age range, prevalence according to sex, cognitive impairment assessment instrument, adherence and cognitive assessment measure, relationship between cognitive impairment and adherence to antihypertensive treatment, main results, and conclusions.

The methodological quality and characteristics of the studies were independently assessed by two researchers, according to the recommendations of the Newcastle-Ottawa Scale (NOS)[28], recommended for evaluation of cohort studies, and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) scale[29], recommended for evaluation of observational studies. Cases of disagreement and/or disagreements were resolved by the involvement of a third reviewer.

RESULTS

The initial database search resulted in the identification of 216 potentially eligible articles for this review. At the end of the evaluation, five articles were included in the final sample, as shown in Figure 1.

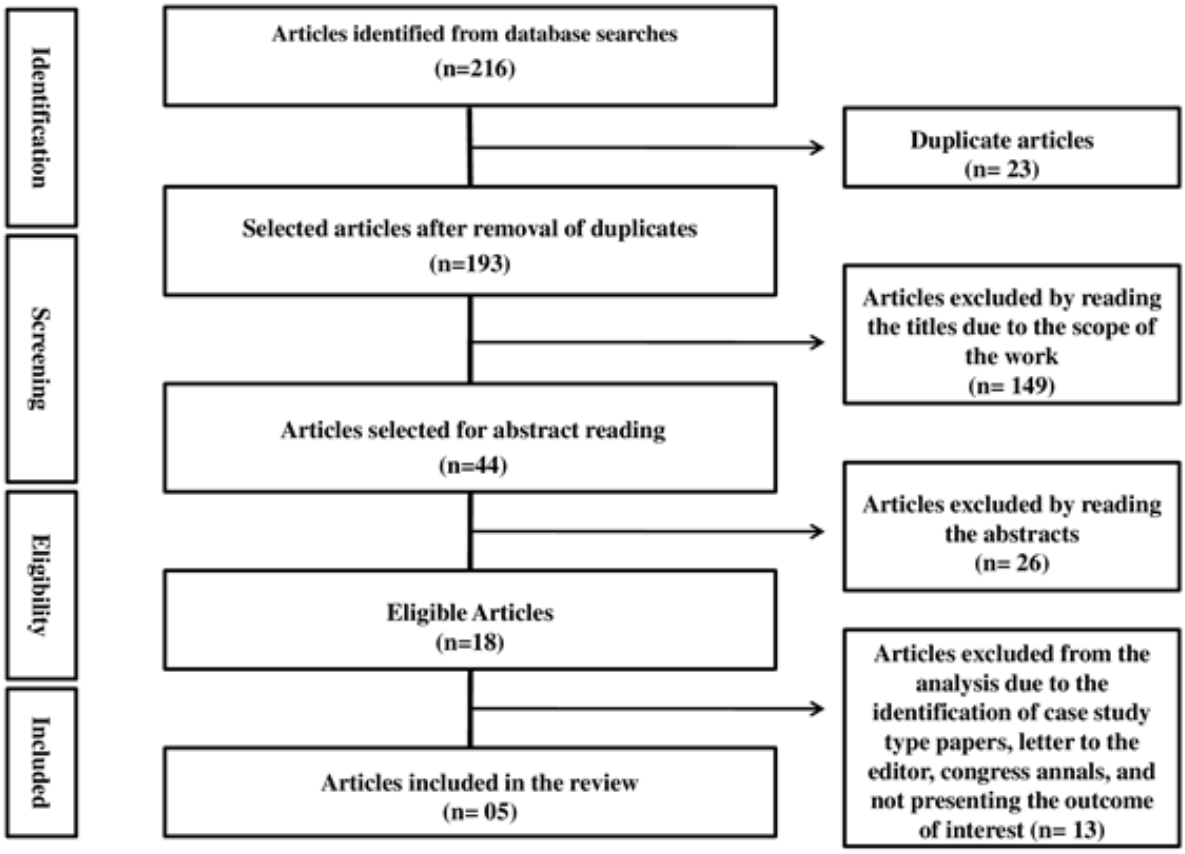

Figure 1 - Flowchart of the article selection process. Teresina, PI, Brazil, 2021.
Source: Authors (2021)

Of the total number of studies included in the review, three (60%) were found in the Pubmed database. Regarding the year of publication, two (40%) studies were published in 2018, one (20%) in 2016, one (20%) in 2015, and one (20%) in 2008. It was found that two studies (40%) were conducted in Poland, one in Korea (20%), one in Brazil (20%), and one in Spain (20%).

English was the language found in most investigations, totaling four articles (80.0%), as was the cross-sectional study design, also found in four publications (80%). The sample/population ranged from 124 to 20,071 aged hypertensive individuals. Females prevailed in all studies, and of the total of 24,052 patients included in the studies, 13,334 (55.4%) were women. Table 1 shows the main characteristics of the studies included in the review.

Table 1 - Main characteristics of the studies included in the review. Teresina, PI, Brazil, 2021 (continues)

Authors and year	Title	Prevalence of SAH, according to gender	Adhesion Measure	Adhesion Measure	Main results
Aiolfi et al.25, 2015	Adherence to medication use among aged hypertensive individuals.	67.7% female	Portuguese version of the Morisky Medication Adherence Scale (MMAS-8)	MEEM	The cognitively impaired aged were more likely to adhere to drug treatment than the non-cognitively impaired aged.
Vinyolis et al.32, 2008	Cognitive function and blood pressure control in hypertensive patients over 60 years of age: COGNIPRES study	55,6% female	Morisky-Green Test (TMG)	MEEM	Significant association between cognitive impairment and low adherence to antihypertensive treatment.
Cho et al.30, 2018	Association between cognitive impairment and poor antihypertensive medication adherence in elderly hypertensive patients without dementia	54,3% female	Cumulative Medication Adherence (CMA)	Prescreening Korean Dementia Screening Questionnaire (KDSQ-P)	Cognitive deficit was associated with poor medication adherence. medication. Cognitive deficit is a possible risk factor associated with low adherence to antihypertensive medication antihypertensive medication, even in patients without dementia.
Chudiak et al.31, 2018	Relation between cognitive impairment and treatment adherence in elderly hypertensive patients	55,7% female	High Blood Pressure Compliance Scale (HBCS)	Mini-Mental State Examination (MEEM)	Cognitive impairment was negatively associated with treatment. We also observed male gender associated with low treatment adherence in hypertensive aged compared with women.

Piotrowicz et al.33, 2016	Subclinical Mood and Cognition Impairments and Blood Pressure Control in a Large Cohort of Elderly Hypertensives	65,6% female	Classification criteria: (1) patients who took regularly, as prescribed; (2) omitted medications 1 to 3 days per month; (3) omitted on 4 to 7 days per month; (4) omitted on 8 to 10 days; (5) omitted on 11 to 14 days: (6) took medications occasionally; (7) did not adhere to treatment in its entirety.	Cognitive Abbreviated Mental Test Score (AMTS) and the Clock Drawing Test (CDT)	Low adherence was related to cognitive deficits. Limitations in the activities of daily living negatively influence medication on medication adherence, which in turn translates into higher BP values.

Source: Authors (2021).

Different instruments have been used to assess adherence to medication for the treatment of hypertension: the Cumulative Medication Adherence (CMA)(30); the High Blood Pressure Compliance Scale (HBCS)(31); the Morisky Medication Adherence Scale (MMAS-8)(25); the Morisky-Green Test (TMG)(32); and one of the articles(33) assessed medication adherence through classification according to regularity of medication use.

Adherence to antihypertensive medications among the aged ranged from 31.5%(25) to 83.6%(30), with better adherence rates in individuals without cognitive impairment in most research. Key information from the studies included in this review is described in Table 1.

Chart 1 - Identification of articles according to authors/year, title, prevalence of SAH, adherence measures and cognitive assessment, main results. Teresina, PI, Brazil, 2021

First Author	Year	Study Location	Language	Type of study	Number of participants
Cho et al.[30]	2018	Korea	English	Retrospective Cohort Study	20,071
Chudiak et al.[31]	2018	Poland	English	Cross-Sectional Study	300
Piotrowicz et al.[33]	2016	Poland	English	Cross-Sectional Study	1988
Aiolfi et al.[25]	2015	Brazil	Portuguese	Cross-Sectional Study	124
Vinyolis et al.[32]	2008	Spain	English	Cross-Sectional Study	1,569

Fonte: Autores (2021).

Studies have found some factors associated with non-adherence to medication among hypertensive aged people, such as cognitive[30,33] and mood[33] deficits, comorbidities such as diabetes, male gender, and low education[31].

To assess cognitive function, three studies (60%)[31-32] used the Mini-Mental State Examination (MMSE). One (20%)(30) of the studies used the Prescreening Korean Dementia Screening Questionnaire (KDSQ-P) and one (20%)[33] employed a combination of the Abbreviated Cognitive Mental Test Score (AMTS) and the Clock Drawing Test (CDT).

The prevalence of cognitive impairment in the aged hypertensive population ranged from 8% to 61.3%, and one of the studies[30] did not record this information.

The relationship between cognitive impairment and low patient compliance to antihypertensive treatment was found in four studies[30-33]. On the other hand, one study[25] showed divergent results, finding that aged hypertensive patients with cognitive impairment adhered more to drug treatment than those without cognitive impairment.

A study conducted in Poland[31] showed that women were more adherent and higher education was associated with greater adherence to antihypertensive treatment. On the other hand, a Brazilian investigation[25] found a significant difference between adherence to hypertension treatment and age group; however, the schooling variable was not observed to influence medication adherence.

Two studies have evaluated the effects of adherence on blood pressure (BP) control in the aged. Results from a study conducted in Spain[32] show that aged with cognitive impairment were 47.0% less likely to comply with antihypertensive treatment and 40.0% less likely to achieve adequate blood pressure control. Similarly, a Polish study[33] found that cognitive impairment was associated with low adherence and, concomitantly, with a greater likelihood of inadequate BP control.

DISCUSSION

This review synthesized national and international studies on the association between cognitive impairment and medication adherence in hypertensive aged, systematically evaluating five articles, which reveals that studies on this subject are still scarce and/or limited, especially in Brazil.

The study is relevant because this is the first systematic review, considering the last 10 years, to investigate the association between cognitive impairment and medication adherence in hypertensive aged people without dementia.

Different instruments were used to assess adherence to hypertension treatment in the studies evaluated: Portuguese version of the Morisky Medication Adherence Scale (MMAS-8)[25]; Morisky-Green Test (TMG)[32]; Cumulative Medication Adherence (CMA)[30]; High Blood Pressure Compliance Scale (HBCS)[31] and classification criteria[33] according to drug administration based on prescribed dosage. In general, these instruments provided a global assessment within the possibilities of each item, since it is important to say that, due to the complexity of the concept and of the factors that interfere with adherence, there is still no method in the literature that is considered the gold standard or comprehensive in its entirety to measure treatment adherence in hypertensive patients.

However, although there is no consensus as to which is the best instrument to measure adherence in hypertensive patients, the most used assessment instruments are those based on the clinical interview[34].

Non-adherence to pharmacological treatment is one of the main factors for inadequate

BP control; therefore, the results of low adherence or non-adherence to medication are worrisome because they can lead to increased morbidity, mortality, and additional costs to the health system[16], especially in aged patients, already vulnerable to risks and susceptible to several comorbidities.

Researchers identified statistically significant differences between genders for non-adherence, indicating low treatment adherence in hypertensive aged males. Moreover, adherence levels were higher in patients with higher education[31]. Hypertensive aged males showed a 0.79-point increase in mean HBCS scale score (p=0.02; CI=0.15-1.43), indicating low adherence among males relative to females. While the mean scores of patients with high education were lower by 1.58 points (p=0.00; CI=-2.57 to -0.59), indicating better adherence in this group[31].

Moreover, studies show that men have greater ignorance about the disease and its treatment, while women have a more accurate perception of their health status and develop greater relationships with the health service[35]. In the case of SAH, low education is an aggravating factor for hindering the recognition of the need for medical assistance and continuity of treatment, whether with medication or not since it is a clinical condition[36].

Although in this study no statistically significant differences were found between income and non-adherence, it should be noted that low income can impact on lower adherence to drug treatment for SAH, since it reflects the scarcity of money to buy medicines, either in situations where the drugs are not purchased due to difficult access to health services[36] or are not available in the basic network.

In this review, different specific instruments were used to assess cognitive function among hypertensive aged individuals, with the MMSE[30-32] being the most widely used in the studies. It is noteworthy that, despite being the most widely used test, there is still no standardization of the use of the MMSE, and the studies adopted different cutoff points to identify cognitive deficit, a factor that hinders the generalization of the results.

The lowest rate of cognitive impairment found was related to a rate of 8.0%[33], while other studies[25-30] showed prevalence above 60% of cognitive impairment in the sample. Studies on the prevalence of cognitive decline in Brazilian aged have presented different estimates, considering the influence of the different socio-cultural and economic context, ranging from 7.1% to 73.1%[37-38]. In international studies, this estimate ranges from 6.3% to 46%[39-40].

The study findings signal the need for the use of tools for early identification of cognitive impairment, since, regardless of the literature, existing concepts agree that aged people with cognitive deficits have a higher chance of developing dementia, especially in cases of recurrent memory loss[41], which can significantly compromise the individual's overall autonomy and, concomitantly, adherence in hypertensive aged people.

Although the influence of cognitive impairment on aged patients' adherence to antihypertensive treatment is still unclear, most studies[30-33] in this review demonstrate a relationship between cognitive impairment and poor medication adherence. The mechanisms by which aged hypertensive patients with CCL have difficulty adhering to medication remain unclear.

It was evidenced that medication adherence among hypertensive aged worsens with a decline in cognitive function[30], even in patients without evident dementia (OR=0.980, p=0.042). The authors point out that the results may be relevant to clinical practice when evaluated from the applicability parameters of the scale used in the study. That is, if a patient scores five on the KSDQ scale (which is just above the cutoff point), then they are likely to have 10% lower compliance than a patient with normal cognition (e.g., score 0 on the KSDQ scale).

In addition, studies[32-33] found that cognitively impaired aged were less likely to

achieve adequate blood pressure control; cognitive impairment was associated with poor adherence and, concomitantly, with a greater likelihood of inadequate BP control.

Cognitive impairment is one of the most important risk factors for low drug treatment adherence in the aged[19], especially when it reflects an inability to prioritize, plan, and organize, in addition to an inability to recall information[18]. The relationship between low medication adherence associated with cognitive impairment can be attributed to several factors, such as unintentional nonadherence[42-43] and forgetfulness[24].

In this review, limitations such as the scarcity of studies on the subject are highlighted, which brings some obstacles regarding the interpretation of the results and should be considered in the discussion.

CONCLUSION

The influence of cognitive impairment on adherence to antihypertensive treatment in the aged was identified in most studies included in this review. Cognitive impairment was associated with low adherence to treatment, thus highlighting the need for early detection to adapt care to the cognitive conditions of the aged, optimize medication management and, consequently, achieve adequate control of BP levels.

The few studies identified limit a broader and more consistent assessment regarding the topic, and additional research is needed to clarify and/or elucidate the results found, as well as to reduce this important gap in adherence to antihypertensive medications.

It can be concluded that, to ensure a safe and appropriate therapy, especially for the aged, it is necessary that health professionals focus their attention and actions far beyond the prescription of therapeutic schemes. It is essential to identify the factors involved in the aging process that may negatively impact adherence to antihypertensive treatment.

Assessing cognitive function and adherence in hypertensive aged people comprises an important step to detect risk factors, understand treatment effectiveness, and implement appropriate strategies to improve adherence and BP control in the aged population.

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Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work - Luz AL de A, Alencar D de C, Macedo JB; Drafting the work or revising it critically for important intellectual content - Luz AL de A, Griep RH, Landim MBP, Alencar D de C, Leal AL de S; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - Luz AL de A. All authors approved the final version of the text.

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