Factors associated with prehospital delay in acute stroke: systematic review

Fatores associados ao atraso pré-hospitalar no acidente vascular encefálico agudo: revisão sistemática

Kaliny Oliveira Peixoto[1], Carlos Eduardo Rocha Correia[2]

1. Graduate student, Medical School, Federal University of Rio Grande do Norte (UFRN), Natal-RN, Brazil.
2. Professor of Neurology, Department of Integrated Medicine, UFRN, Natal-RN, Brazil.

ABSTRACT

Purpose: Stroke is a major cause of death and disability worldwide. Although thrombolytic therapy is effective, it is still underutilized mainly due to delays in patient assistance. A systematic literature review was made to identify the main factors associated with prehospital delay. **Methods:** A MEDLINE-Pubmed database search in February 2016 retrieved 896 articles, of which 6 were selected for analysis. **Results:** Low educational level was identified as the most important factor of delay. Means of transportation, transfer between hospitals, as well as onset of symptoms at home were also relevant. **Conclusion:** We conclude that educational policies and facilitated access to hospital care are keys to minimize barriers to early stroke treatment.

Key words: Stroke, Acute. Prehospital emergency care. Health education. Thrombolytic therapy.

RESUMO

Objetivo: O acidente vascular encefálico (AVE) é uma das principais causas de mortalidade e incapacidade em todo o mundo. O tratamento trombolítico, embora eficaz, é ainda pouco utilizado devido principalmente ao atraso no atendimento dos pacientes. Por intermédio de revisão sistemática, procuramos identificar os principais fatores responsáveis por esse atraso. **Métodos:** A busca realizada na base de dados MEDLINE em fevereiro de 2016 identificou 896 artigos, dos quais 6 foram selecionados para análise. **Resultados:** Baixo nível educacional foi identificado como o fator mais importante. O meio de transporte, a transferência entre hospitais e início dos sintomas em domicílio também foram relevantes. **Conclusão:** Concluímos que a implementação de políticas públicas voltadas à educação e maior acessibilidade à assistência hospitalar são medidas fundamentais para minimizar as barreiras ao tratamento do AVE.

Descritores: Acidente vascular encefálico. Assistência hospitalar. Educação em saúde. Terapia trombolítica.

INTRODUCTION

Stroke is defined as a focal, sometimes global neurological deficit of sudden onset, lasting longer than 24 hours (or leading to death), of presumed vascular origin. It can be subdivided into ischemic stroke and hemorrhagic stroke, the latter comprising intracerebral or subarachnoid hemorrhages. The stroke is a multifactorial disease, having as main causes systemic arterial hypertension, diabetes and smoking[1].

Stroke is the second leading cause of death worldwide, responsible for nearly six million lives lost each year. Developing countries have the highest rates of stroke deaths in the world, accounting for more than two-thirds of deaths[2]. In Brazil, the stroke has become a leading cause of death and disability. Among all Latin American countries, it is the country with the highest mortality rates[3].

Among developing countries, the incidence of this disease has more than doubled, from 52 to 117 cases per 100,000 people per year[4]. It is estimated that in 2030 the number of cases in the world increases to over 30 million per year. This growth will be attributed to the increase in the number of cases among developing countries, while the incidence of the disease in developed countries should remain stable[5].

Stroke is a medical emergency and requires the attention of a specialist whose care significantly decreases mortality and morbidity rates, and urgent intervention follows alongside general measures[6]. The objectives of the initial evaluation are: confirmation of the diagnosis and etiology (hemorrhagic or ischemic), identification of the time of onset of symptoms and their evolution, and graduation of the intensity of the neurological deficit. All these aspects are decisive in the decision to use thrombolytic therapy with recombinant tissue plasminogen activator (rtPA) in stroke. Emergency care includes stabilization of the patient's vital conditions, such as respiratory care, hydroelectrolyte balance, hemodynamic monitoring, dietary conditions, temperature, blood glucose control, and prevention of deep venous thrombosis[7].

Thrombolytic therapy is an effective treatment, which reduces neurological impairment and improves the survival of patients[8]. Such effectiveness is proven by the application of scales that measure this commitment. They are also useful in monitoring the evolution of patients' clinical status, anticipating their prognosis. The most commonly used scales to assess stroke impairment are: Rankin's Scale, National Institute of Health Stroke Scale (NIHSS) and Barthel's index[9].

Thrombolytic therapy requires the presence of an experienced physician to evaluate the inclusion and exclusion criteria, an adequate environment for monitoring neurological signs, vital signs (especially blood pressure), and hemorrhagic complications during and after rtPA infusion. Further research should be done to determine the etiological mechanism and choice of the best secondary prophylaxis therapy[10].

Although effective, thrombolytic therapy is performed in relatively few patients[11]. This situation stems mainly from the narrow therapeutic window for administration of the drug (up to 4.5 hours after the onset of symptoms), which makes early diagnosis fundamental[12]. Other factors that contribute to the underuse of the therapy are: lack of knowledge about the treatment or fear of hemorrhagic complications. A literature review has attempted to understand which factors limit doctors' adherence to guidelines, pointing to organizational barriers, patient-related factors, the guideline implementation process and their characteristics[13].

Prehospital delay has been considered the major cause of delay in the treatment of stroke[14]. It has been decisive the low level of knowledge about the emergency medical services and the availability of acute stroke treatment in Brazil[15]. Data on the assessment of stroke care in developing countries are scarce and most available studies cover urban areas in which health care systems have reasonable resources. The quality and quantity of care is irregular in developing countries, with areas of excellence mixed with areas of serious need, depending on the patient's location, socioeconomic status, education and cultural beliefs[2]. Studies in developed countries have concluded that interventions are needed to increase the number of patients eligible for acute stroke, such as educational campaigns aimed at immediate recognition of warning signs, contributing to proactivity to rescue the victim of stroke[16].

In view of the explicit importance of this clinical entity, the present study aims to reveal the main obstacles faced by patients suffering from stroke to obtain hospital care. Thus, it is expected that the results of this research contribute to the search for strategies that minimize these barriers, providing adequate treatment and a better quality of life for the victims of this disabling disease.

METHODS

This is a systematic review. The search was performed in the MEDLINE / PubMed database and, in the search, the following key words were used: stroke, cerebrovascular disease, illness, delay, lag, time, pre-hospital, presentation hospital, arrival. In the tracking of the publications, the logical operators "AND" and "OR" were used, in order to combine the key words mentioned above. Restricted filters to human studies, published in English and Portuguese were used.

The following inclusion criteria were considered: a) observational and interventional studies; b) evaluation of acute stroke patients; c) identification of factors that contribute to the pre-hospital delay; d) publication period: 1995 to 2016; e) correlation of the delay with variables of multiple categories (clinical, socioeconomic, demographic and structural).

The following were excluded: systematic review studies; with restriction of age or sex; with less than three factors to the identified delay; with only one category of analyzed variables. The selection of the studies was then performed in three stages: 1st step - reading the titles; 2nd step - reading the summaries of the selected articles in the 1st step; 3rd step - reading in full of the selected articles in the 2nd step. From the selected studies, the following aspects were analyzed: a) local; b) sample; c) type of study; d) applied methodology; and e) results. The search in the database occurred between February 9 and 21, 2016.

RESULTS AND DISCUSSION

From 896 articles obtained in the initial search, 33 were selected after reading the titles (1st stage); from these, 26 were excluded after reading the abstracts (2nd stage), since they did not fully meet the inclusion criteria.

Therefore, seven papers were read in full (3rd stage), and one article was excluded, which was in disagreement with the inclusion criteria[14]. At the end, the total of six papers was reached. The selection process of the articles is presented in Figure 1 and the references of the six studies analyzed are shown in Table 1.
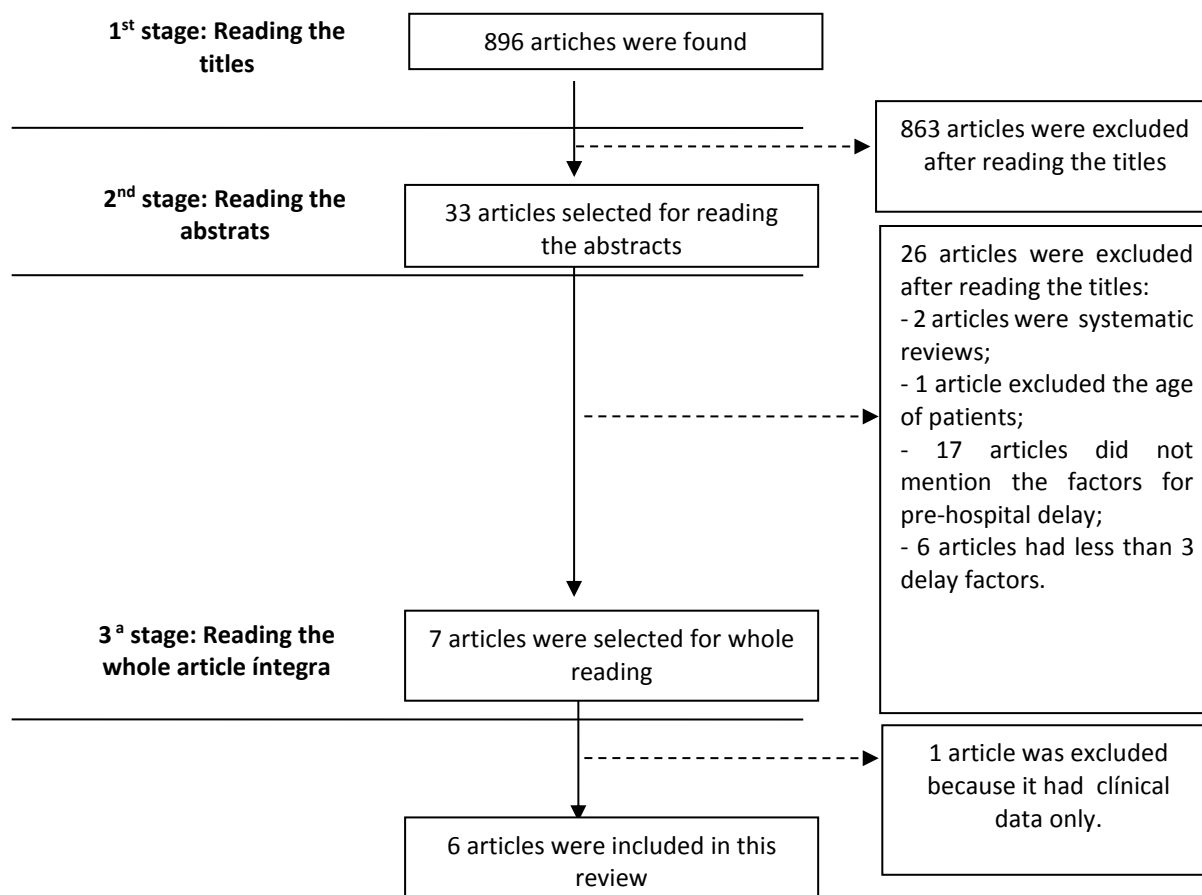
Figure 1 – Selection process of published articles on the factors that influence the prehospital delay in stroke victims

Table 1 – Articles used in this review.

Author, year	Country	Sample	Type of study
JIN et al., 2012	China	6102	Analyt Obs Prosp
HONG et al., 2011	South Korea	184	Analyt Obs Prosp
CHEN et al., 2007	Taiwan	129	Analyt Obs Prosp
TAN, CHANG E LIOU, 2002	Taiwan	197	Analyt Obs Prosp
LACY et al., 2001	USA	553	Analyt Obs Prosp
AZZIMONDI et al., 1997	Italy	189	Analyt Obs Prosp

Analyt: Analytical; Obs: Observational; Prosp: Prospective

The studies were published between 1997 and 2012, all of which were observational and prospective. Two of them were held in Taiwan, while the others covered

China, South Korea, the United States (USA, New Jersey) and Italy. Samples ranged from 129 to 6102. The methodology applied and the results obtained from the studies can be seen in Table 2.

Table 2 – Methodology of the studies used in this review.

Author, year	Metodology	Results
JIN et al., 2012	Variables of interest: sociodemographic, socioeconomic, education, initial simptoms, transportation, past pathological history e clinical history.	Advanced age and ambulance use (early arrival). Delay factors: age; onset of symptoms at home, past history; mild symptoms; transfer between hospitals.
HONG et al., 2011	Variables: age; sex; education; time of onset, type, change and recognition of symptoms; severity of the stroke; reference between institutions; Living alone	Advanced age (early arrival). Delay factors: symptoms at home; aggravation of symptoms; other institutions.
CHEN et al., 2007	Variables: age; sex; education; symptoms upon waking; transportation; Previous stroke; gravity; initial symptoms; other institutions.	Advanced age, ambulance and previous stroke (precocious). Delay: age, lower educational level, waking and mild symptoms; interhospital transfer.
TAN, CHANG E LIOU, 2002	Variables: age; sex; educational level; type of transport; place of residence; other associated diseases; family history and type of stroke; referral from another hospital; clinical manifestations; Living alone.	Use of ambulance (early arrival). Delay factors: advanced age; late recognition of symptoms; mild symptoms; interhospital transfer.
LACY et al., 2001	Variables: demography; mode of transport; history of cardiovascular disease; hospital complexity; time of evaluation.	Advanced age, ambulance and previous stroke (early arrival). Factors of delay: race; younger; other transport.
AZZIMONDI et al., 1997	Variables: age; sex; symptoms upon waking; area of residence; gravity; level of consciousness; invalidity.	Delay factors: waking, mild symptoms. Educational measures: clinical efficacy.

Sociodemographic variables were analyzed in all studies. No author found a significant correlation between the prehospital delay and the patient's gender. Hong et al., 2011; Chen et al., 2007 and Lacy et al., 2001 found an association between advanced age and early hospital admission. Such finding was attributed to the presence of comorbidities and previous experience, increasing the propensity to perceive the symptoms as an emergency. The inclusion of patients from well-organized elderly institutions in the American study may have contributed to the outcome. Jin et al., 2012 found a trend towards earlier hospital admission in patients 65 years of old or older, attributed to the increased awareness about the symptoms of stroke in this age group, the target of health promotion campaigns. Differently, Tan et al, 2002 reported a higher age in the group of patients with prehospital delay of more than 2 hours. The authors stated that in Taiwan the population, especially the elderly, is reluctant to seek medical assistance, believing that the symptoms will disappear spontaneously. Azzimondi et al., 1997 found no association between the variables.

Only Lacy et al., 2001 found a relevant association with race, noting that black people take longer to reach the emergency unit, with a lower propensity to use ambulances than white people. This result may be related to the difficulty of prehospital care offered to black people in this population.

Education was evaluated by most articles. Chen et al., 2007 and Tan et al, 2002 found an association of lower educational level with delays in the search for medical care, explained by the lack of recognition of the severity of the symptoms. Only Jin et al., 2012 and Hong et al., 2011 did not find an association between education and backwardness. This result, incongruent with other studies, may be justified by the inclusion of only patients from urban areas, a sample with a higher and more homogeneous educational level, different from that expected in rural and remote areas. Lacy et al., 2001 and Azzimondi et al., 1997 did not evaluate education. However, the second study stated that educational programs could guide the early search for medical care and could double the number of patients eligible for thrombolytic treatment in the population.

The evaluation of the initial symptoms was performed by Jin et al., 2012; Hong et al., 2011; Chen et al., 2007; and Azzimondi et al., 1997. The first two studies found an

association between the onset of symptoms at home and the prehospital delay, justified by the greater possibility of assistance by witnesses in a public place in comparison with the residence. The last two studies found association of delay with symptoms on waking. Determining bedtime for the onset of symptoms may have contributed to overestimate the delay.

The mode of transportation was not evaluated by Hong et al., 2011 and Azzimondi et al., 1997. Other studies found an association between ambulance use and early arrival to emergency, while other forms of transportation contributed to the prehospital delay.

As for the previous pathological history, Tan et al., 2002 did not find prior stroke association with the delay. Jin et al., 2012 associated the presence of previous stroke, transient ischemic attack, systemic arterial hypertension and hyperlipidemia to prehospital delay, denoting misperception of symptoms or neglect of the experienced health condition, corroborating with the need to promote education. On the other hand, Chen et al., 2007 and Lacy et al. associated the previous stroke with the early arrival to the emergency service, attributed to the previous knowledge of the symptoms, facilitating the perception of the manifestation of the disease. In the above studies, the presence of previous cardiovascular diseases was associated with an early arrival to the hospital. The increased knowledge and fear of heart disease may be a factor that drives patients to seek medical help more quickly. Hong et al., 2011 did not include patients with prior comorbidities in there study. Azzimondi et al., 1997 did not analyze this variable.

Except for Lacy et al., 2001, the other authors evaluated the clinical characteristics of stroke, finding an association between the lower intensity of symptoms with the longer prehospital delay. Jin et al., 2012, showed that patients with haemorrhagic stroke and those with lowered level of consciousness took less time to seek hospital care. The perception of urgency associated with greater severity of symptoms may have contributed to the finding. The studies of Tan, at al., 2002 and Azzimondi et al., 1997 corroborate this analysis. Chen et al., 2007 showed that the delay was higher in patients with NIHSS (severity rating of stroke) score classified as mild or moderate. Hong et al., 2011 evaluated the time of onset, type, change and recognition of symptoms, and worsening of symptoms. The

presence of the latter showed an association with prehospital delay, more probably reflecting the inadvertent waiting for the spontaneous improvement of the symptoms.

Hong et al., 2011; Chen et al., 2007 and Tan, et al., 2002 assessed the need for reference among health institutions and found association with the delay. Initial care in the nearest units, by a general practitioner, in less equipped units contributes to the delay of thrombolytic treatment. Surprisingly, Hong et al., 2011 and Tan, et al., 2002 found no association between living alone and delayed care. The interference of other variables, such as presence of more severe symptoms, ambulance use, and early recognition of symptoms may have contributed to this finding.

Considering the above mentioned, the most efficient way to reduce the prehospital delay in stroke victims is to develop educational strategies, instructing the population to recognize symptoms early, seeking to arrive as soon as possible through ambulance rescue request to the emergency service trained within the therapeutic management for the performance of thrombolysis. This management will provide a better quality of life for patients. Other measures should also be implemented to facilitate access to hospital care, such as increased investment in emergency transportation and staff training. The main limitation of this systematic review is the use of only one database, with a disproportionate representation of Asian studies and lack of studies in African and South American territory. Conducting research with other populations, including Brazilian, it is important to evaluate the local factors related to the delay in the treatment of stroke.

CONCLUSION

The present study revealed, through the analysis of the selected studies, that the non-recognition of the characteristic symptoms of stroke or the late perception of this symptomatology correspond to the main factor of prehospital delay. This association is clearly related to the need to develop an educational program that allows the early recognition of symptoms. We conclude that educational policies and facilitated access to hospital care are keys to minimize barriers to early stroke treatment.

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