Migraine: etiology, risk, triggering, aggravating factors and clinical manifestations

Migrânea: etiologia, fatores de risco, desencadeantes, agravantes e manifestações clínicas

Migraña: etiología, factores de riesgo, desencadenantes, agravantes y manifestaciones clínicas

Natália Lindemann Carezzato[1], Priscilla Hortense[1]

This study aimed to identify the etiology and clinical manifestations of migraine. An integrative literature review was performed guided by the question: What is the evidence available in the literature about the etiology, signs and symptoms of migraine? The article search was conducted in the electronic databases PubMed and LILACS, considering publications in the period from 2006 to 2010. The selected articles were categorized and evaluated according to the level of evidence. One found 1,677 articles and 26 were selected for full reading. Most studies (84.6%) consisted of a non-experimental design and were classified as evidence level IV. Although the clinical manifestations found in this study confirm the data available in the literature, it is noticed that migraine does not have well-established causes.
Descriptors: Headache; Causality; Signs and Symptoms; Migraine Disorders.

Este estudo objetivou identificar a etiologia e as manifestações clínicas da migrânea. Foi realizada revisão integrativa de literatura norteada pela questão: quais as evidências disponíveis na literatura sobre a etiologia e os sinais e sintomas da migrânea? A busca de artigos foi conduzida nas bases eletrônicas PubMed e LILACS, contemplando publicações do período de 2006 a 2010. Os artigos selecionados foram categorizados e avaliados segundo o nível de evidência. Foram encontrados 1.677 artigos, sendo selecionados 26 para leitura na íntegra. A maioria dos estudos (84,6%) consistiu em delineamento não experimental, sendo classificados com nível de evidência IV. Apesar das manifestações clínicas encontradas neste estudo confirmarem os dados disponíveis na literatura, nota-se que a migrânea ainda não possui suas causas devidamente estabelecidas.
Descritores: Cefaleia; Causalidade; Sinais e Sintomas; Transtornos de Enxaqueca.

El objetivo fue identificar la etiología y las manifestaciones clínicas de la migraña. Fue realizada revisión integradora de la literatura por medio de la pregunta: ¿cuáles evidencias están disponibles en la literatura acerca de la etiología y los signos y síntomas de la migraña? La búsqueda de los artículos se realizó en las bases electrónicas PubMed y LILACS, y abarcó publicaciones del período 2006-2010. Los artículos seleccionados fueron clasificados y evaluados de acuerdo con el nivel de evidencia. Se encontraron 1.677 artículos y 26 fueron escogidos para lectura completa. La mayoría de los estudios (84,6%) consistió en el diseño no experimental, clasificados con nivel de evidencia IV. Las manifestaciones clínicas encontradas en este estudio confirman los datos disponibles en la literatura, pero se percibe que la migraña aún no posee causas debidamente establecidas.
Descriptores: Cefalea; Causalidad; Signos y Síntomas; Trastornos Migrañosos.

[1]Universidade Federal de São Carlos. São Carlos, SP, Brazil.

Corresponding author: Natália Lindemann Carezzato
Rua da Aspereza, 148 - CEP: 05180-030. São Paulo, SP, Brazil. E-mail: nahcarezzato@gmail.com

Introduction

Headaches are a major public health problem in Brazil and in the world, due to their individual, work and social impact. Being one of the most common chronic manifestations[1], headaches require great attention from health authorities and public policies regarding its prevention, diagnosis and treatment[2].

Regarding the criterion for the classification of headache, according to its etiology, two groups were found. Primary headaches are those that do not have apparent etiology by standard clinical or laboratory tests, such as migraine, cluster headache and tension-type headache. Secondary headaches present pain as a result of aggressions to the body, caused by diseases shown by clinical or laboratory tests such as meningitis, poisoning, systemic infections, among others[3].

Migraine, classified within the group of primary headaches, is a "neurovascular disorder characterized by repeated attacks of headache that may occur with a highly variable frequency"[4:2], varying from a few attacks during life to numerous episodes per month.

Migraines can be classified into two groups: with and without aura. The migraine without aura is characterized as common migraine[5], as hemicranial or bilateral pain, with variable intensity (moderate to severe), with a throbbing character, which presents clinical deterioration after the performance of daily functions and that may be accompanied by other symptoms. The length can be from 4 to 72 hours, and may recur after analgesics[6].

The migraine with aura is characterized by transient focal neurological symptoms before the onset of pain that settles gradually. It usually last around 5-20 minutes not exceeding 60 minutes[5], and the symptoms can be: flickering lights, spots, loss of vision, tingling and numbness. It is common for migraineurs to present its two types[6].

Premonitory symptoms occur in up to 48 hours before migraine attacks, in most patients, being the most common: mood changes, sleep disturbances,

photophobia, phonophobia, intestinal disorders, fluid retention, desire or revulsion for specific foods, among others - which often impede the implementation of routine activities[5].

In a study conducted in six Latin American countries, the lowest prevalence of migraine with or without aura, was identified in Argentina, and the highest for women in Brazil. It is noticed that migraines affects mainly women, generally between the ages of 30 to 50 years old[7].

It is known that migraines cause a high impact on quality of life. A review study[8] found out that treatments for migraine that improve Quality of Life are drugs used during the crisis and prophylactic, as well as non-pharmacological measures. However, the increased knowledge about the causes, risk, triggering and aggravating factors enables a care planning aimed to avoid these factors and thus episodes of migraine.

When considering pain as an important human response, one must understand it as a unique, subjective and complex experience and that its perception involves many factors that can soften or intensify this experience.

Thus, the assessment and measurement of the painful experience are essential for the study of the mechanisms involved and for its proper management[9], as well as the understanding of the causal factors and the characteristics of the phenomenon. It is observed that there is an important gap in the knowledge of the causal factors of migraine; knowing what these factors are provide the healthcare team with an understanding capable of producing appropriate management actions for this type of pain.

Since no laboratory tests can allow a correct diagnosis of migraine, the most accurate information on this problem is reported by the patient, being important to conduct a good, thorough anamnesis and careful listening[3]. Thus, the proper evaluation of individuals with migraine becomes something essential for its diagnosis, management and care planning.

Given the above, it is important to conduct

an approach about the elements of migraine. Thus, this study aimed to identify, through an integrative literature review, the etiology and clinical manifestations of migraine.

Method

An integrative literature review[10-11] was conducted, a research method that provides a knowledge synthesis and the incorporation of the applicability of results of significant studies carried out in practice. The primary purpose is to deepen the understanding of a given phenomenon and highlight possible gaps, enabling critical thinking that the practice needs. It consists of 5 stages[10-11], which are: problem identification, establishment of criteria for sample selection, studies categorization (data collection) by means of reading in full all the items selected in the previous phase, analysis and data interpretation and synthesis of knowledge.

After identifying the problem, it was established the following guiding question "What is the evidence available in the literature about the etiology, signs and symptoms of migraine?".

In the second phase, the sample selection criteria were established, and the search for articles of interest was performed in the electronic databases of PubMed, provided by the U.S. National Library of Medicine (NLM), and LILACS, offered by the Latin American and Caribbean Health Sciences Information Center (BIREME).

The keywords "migraine disorders" found in the *Descritores em Ciências da Saúde* (DeCS) [Health Sciences Descriptors], was used for searches in LILACS. For searches in PubMed, the descriptors used were "migraine disorders" and "signs and symptoms" and the subheading "etiology", found in the Medical Subject Headings (MeSH); on this database, the crossings were "migraine disorders" AND "signs and symptoms" and "migraine disorders" AND "etiology".

For the articles selection, one considered publications concerning the period from January 1,

2006 to December 31, 2010, being a total of 5 years.

Identical studies found in different databases or different descriptors intersections were considered only once.

The inclusion criteria were: articles that demonstrated, in its abstract, the study of related factors (etiology) and defining characteristics (signs and symptoms) of migraine; original articles; articles whose research subjects were human beings and contemplated ages equal to or above 18 years old; articles presented in English, Portuguese and Spanish. The exclusion criteria adopted were: articles which are unavailable online and in full or not accessible in the libraries where the researchers had access to; and articles that did not answer the main question established for the research.

The publications were pre-selected after reading and analysis of the abstracts, according to the inclusion and exclusion criteria previously established. One elected the articles that addressed relevant subjects to the purpose of this study and the research question previously defined.

To extract the data from the articles elected, a meticulous analysis was conducted after their full reading. For this, one used an adapted instrument from another one available in the literature[12-13]. This instrument allowed one to collect and store data such as the article's and the journal's name, the database where the item was found, the authors, as well as their country of origin and place of work, the year and area of publication, the objectives, the methodological characteristics of the study (methodological approach) and the results achieved (etiology, signs and symptoms). In the last item other unanticipated results were found, which was probably not wise to discard (risk, initiating and aggravating factors). Furthermore, the instrument enabled one to collect the evidence level of the study.

Each study was classified according to its level of evidence[14], which classifies studies into six levels of evidence power according to their design, namely: Level I - meta-analysis, Level II - experimental study,

Level III - quasi-experimental study, Level IV – non-experimental study, level V - case report and level VI - opinion piece. In order to analyze the level of evidence of each article it was necessary an attentive and detailed reading of the research method used by the authors.

Each selected article was read and categorized, the data were organized into tables, compared, and finally performed the synthesis of the knowledge produced, providing discussion of major findings and subsequent conclusions.

Results

The total number of articles found in the search was 1,677. After using the inclusion and exclusion criteria, 26 articles were chosen to compose the integrative literature review. When performing full reading of the chosen articles, it was observed the appearance of other important factors as well as the etiology, symptoms and signs. Due to the importance and relevance of such elements, one chose to include them as valid results in this study, being them the risk, initiating and aggravating factors of migraine.

The only causal agent of migraine found in this integrative literature review was genetic predisposition[15-18]. Risk and triggering factors, signs and symptoms of migraine found in this review are shown respectively in Figures 1, 2 and 3.

Groups	Risk factors
Related to gender	Female[15,19-20]
Related to skin color	White[19]
Related to emotional and psychological aspects	Child maltreatment: physical abuse, physical neglect, emotional neglect, and particularly, emotional abuse[21] Personality traits and psychosomatic mechanisms[22]
Related to hormonal factors	Hormonal contraceptive use[19,23] Hormonal changes[24]
Marital status	Married[15,25]; widow[15]
Others	Helicobacter pylori infection[26] Hyperinsulinemia in non-obese patients[27]

Figure 1 - Risk factors for migraine found through the integrative literature review, n=26

Groups	Triggering factors
Emotional and psychological aspects	Stress and anxiety[24,28]; psychological factors[15]; fatigue and mental exhaustion[15,25]
Physiological aspects	Muscle tension in the neck[25]
Environmental aspects	Changes in the atmospheric temperature[24]; Air pollution[29-31]
Sensory stimuli	Smells/odors, perfumes in general and feminine ones, cigarette smoke, smell of food, gasoline, incense, coffee[24-25,32] Noise[24]; starvation[28]; vestibular stimulation and induced vertigo[33]
Feeding	Fasting[34]; chocolate and cheese[24-25]; beer and spirits[24]; red wine[24-25]
Sleep pattern	Rhythm of sleep[15,25]; sleep deprivation and prolonged sleep[28,34]
Hormonal	Menstruation[25]
Habits	Hair washing or showers; exposure to sunlight; association of hair washing with exposure to sunlight, sit down in the breeze of the fan/air conditioner or applying henna hair dye[34]

Figure 2 - Triggering factors of migraine found through integrative literature review, n=26

Groups	Signs and symptoms
Type of pain	Pressure and stab (chronic migraine)[16,35]; throbbing (migraine with and without aura)[16,18-19,28,36]; Unilateral[28]; bilateral, which may persist to the left or to the right[16,18]
Duration of pain	Peak attack from 4 to 6 hours[15]; average duration of the crisis from 5 to 12 hours[16,18,28]
Severity of pain	Moderate to severe[16,24]
Location of pain	Temporal, frontal, eyes and occipital region (less frequent)[16,24,36]
Start and frequency of seizures	14 to 16 years old, on average[16,18]; 3 days in the last month, on average[16,24]
Episodic pattern	Fixed in the afternoons, evenings or weekends[16,28]; women in the menstrual period[16]
Sensory stimuli	Phonophobia and photophobia[16,18,24,28,35,37]; paresthesia[36]; dizziness and vertigo[28,37] Osmophobia: perfumes (female ones and deodorants), food (coffee, fries and onions), cigarette, others (gasoline and detergent)[24,28,32]
Related to quality of life	Occupational, academic, domestic and social disability associated with migraines[16,19]; tiredness, irritability, tension[16,36]; depression[16-17,22,37-38]; loss of libido[16]; stress and anxiety[17,37-38]; insomnia and sleep disorders[16,37]
Gastrointestinal disorders	Anorexia[16], nausea and vomiting[16,18,24,28,35,37]; upper abdominal pain and dyspepsia[39]
Other symptoms	Migraine with aura and chronic one: focal neurological symptoms and visual auras[16] After the headache: tiredness, drowsiness, irritability and depression[16]

Figure 3 - Signs and symptoms of migraine found through integrative literature review, n=26

Some studies have found the existence of aggravating factors of pain, ie, factors that intensify pain when they happen. The aggravating factors of pain identified were physical activities such as walking, climbing stairs or carrying weight[16,18-19,28], noise or presence of light[19] and kinesiophobia[40].

Regarding the level of evidence, the majority of the studies (84.6%) consisted of non-experimental design, being classified as level of evidence IV. The other studies (15.4%) consisted of studies of experimental design (Table 1).

Table 1 - Distribution of the selected studies according to their design, level of evidence and percentage

Design	Level of evidence	n (%)
Non-experimental design[15-20,22-28,32-40]	IV	22 (84.6)
Quasi-experimental design[21,29 to 31]	III	4 (15.4)
Total		26 (100.0)

Discussion

This research found out that there are few studies on the etiology of migraine, which is still unknown and poorly described in the literature. The little knowledge about the causes of migraine makes it hard a correct diagnosis and the selection of a treatment that is really effective and focused on its causal agent. It was observed that people with chronic daily headaches show a substantial genetic predisposition[15-18].

About the risk factors, some authors, in order to determine the distribution and prevalence of migraine in adults, its determinants and clinical characteristics, indicated the female sex as prevalent for this chronic disease[15,19]. It was also observed that this fact is possibly due to hormonal changes that affect women during their menstrual cycle, which is a risk factor for migraine[19-20].

Other authors report that, although they did not find any differences in the mechanisms of genetic factors for migraine among men and women, women may have an increased risk in their expression of pain when exposed to endogenous and exogenous triggering factors[20]. Also, there is an association between migraine and white skin, which may be due to a genetic vulnerability of the individual[19].

In a recent study of cross-sectional design, with the aim of evaluating the relationship among childhood abuse, neglect and characteristics of migraine, the authors found out that childhood maltreatment, especially emotional abuse, is one of the factors that could characterize risk to the onset of chronic migraine, but other categories of trauma may also be associated[21].

Authors report the association between hormonal contraceptive use and the prevalence of migraine[19,23]. They also showed an increased prevalence of headache, especially migraine, among previous or current users of oral contraceptives, and for current users, there is a higher prevalence among the ones composed by estrogen[23]. In another study, the authors found headache as a common symptom reported by women in the climacteric syndrome, among others[41].

Also regarding risk factors, it was observed that the infection by *Helicobacter pylori* would be a probable independent environmental risk factor for migraine without aura, especially in patients who are not hormonally or genetically susceptible to migraines[26].

Regarding triggering factors, the emotional and psychological aspects that can trigger migraine are tiredness, mental exhaustion, stress and anxiety, besides other psychological factors[15,24-25,28]. Besides these, environmental aspects, such as the change of atmospheric temperature, hormonal changes[24] and menstruation[25], may also influence the onset of the disease.

An interesting fact concerns the induction of migraine attack triggered by odors[24-25,32], generating hypersensitivity particularly in women[24]. The intolerance to odors, besides being a triggering factor, can also be considered a clinical manifestation during seizures[32].

Regarding sensory stimuli, it may be mentioned

olfactory stimuli associated with a history of osmophobia, such as perfumes in general and female ones, cigarette smoke, smell of food, incense, coffee, gasoline, and others[32]. Still within this group, there are other factors such as noise[15,25] and hunger[28].

Related to food, not eating[34] as well as the consumption of certain foods and beverages can trigger attacks of migraine, and the main food and drinks that appeared in the surveys were chocolate, cheese, red wine[24-25], beer and spirits[24].

It is known that the clinical condition of carrying a chronic disease can affect significantly the quality of sleep, highlighting its impact on the daily life of every individual. Not only as a result of the disease, but also sleep deprivation and prolonged sleep may be triggering causes of migraine[15,28,34].

Also related to the quality of life and lifestyle, one can add importance concerning the habits of life of each individual. An unpublished prospective study was conducted with 1,500 Indians diagnosed with migraine (with and without aura), and in 94 individuals in total, hair washing or showers were mentioned as an unusual triggering factor for migraine. The association of hair washing with exposure to sunlight, sitting down in the breeze of the fan/air conditioning or applying henna hair dye were other triggering factors mentioned[34].

Another important factor mentioned in this review referred to air pollution as a triggering factor for migraine[29-31]. Some authors indicated as triggering factors of migraine for women in the period of heat, exposure to sulfur dioxide (SO_2), and in the cold season, to the particles of matter smaller than 2.5 μm; for men, in the period of heat, the triggering factors of migraine were exposure to nitrogen(NO_2) and carbon monoxide (CO)[29,31]. Unlike these, another study found out that, for women, in the cold season, the main triggering factor was sulfur dioxide(SO_2)[30].

During this integrative literature review, it was observed that there is a larger number of results regarding the signs and symptoms of migraine than for other topics surveyed.

Regarding the group related to the type of pain, one found the pulsatile types[16,18-19,28,36], pressure and stabbing types[16,35], unilateral[28] and bilateral, which may persist to the left or to the right[16,18].

As to the duration of the pain, the peak described of migraine attack is from 4 to 6 hours[15], and the average duration of attacks can vary between 5 and 12 hours[16,18,28], with the frequency of seizures from one to three times a month[16,24].

It is known that the experience of pain is subjective and that its threshold can vary for each individual. In this sense, different intensities of pain were detected for patients with migraine, being found pain severity from moderate to severe[15-16,18,24,35,38].

Regarding the location of pain, most incidents happened at the temporal, frontal, occipital and eye regions[16,24,36], with the onset of migraine attacks around 14 to 16 years of age, on average[16,18].

The largest group among the signs and symptoms found in this review describe findings with regard to sensory stimuli, being the most frequent photophobia and phonophobia [16,18,24,28,35,37], dizziness, vertigo (mild, moderate and severe) and paresthesias[35-37]. Among these, another important and apparent sensory stimulus in the integrative literature review is osmophobia[24,32,35]. As for odors themselves, the most frequent were female perfumes and deodorants, food (coffee, fried food and onions) and cigarettes, among others, such as gasoline and detergent[32].

In the group of gastrointestinal disorders, were also found: anorexia, diarrhea, nausea and vomiting[16,24,28,35,37]. Complementing these findings, another study assessed the prevalence of idiopathic upper abdominal symptoms in patients with migraine, comparing them with a healthy control population; one also found upper abdominal pain and dyspepsia[39].

One also observed symptoms after the crisis of headache such as fatigue, drowsiness, irritability and

depression[16].

This study has some limitations. One of them was the use of the term "etiology", which is a subheading and not a controlled descriptor, for searching in the PubMed descriptor. Another factor was the time frame of the review, between 2006 and 2010, because it is possible that other studies were published outside this period.

Conclusion

This study highlights important elements about migraine, enables one to deepen their knowledge and thus rethink the care planning for the person with this type of chronic pain in professional Nursing practice from a thorough and individualized assessment of the person with migraine, including anamnesis and history of pain, nurses can establish, with the client, modifiable risk factors, in addition to triggering and aggravating factors, indicating strategies to avoid these factors, as well as the crises - or minimize them.

Other studies on the origins of migraine are still necessary, since it does not have well-established causes yet. This fact makes it difficult to find strategies to prevent its occurrence.

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Carezzato NL and Hortense P contributed to choose the research problem, identification of objectives and methods to be used, collection, analysis and data interpretation, writing of the article, critical revision and final approval of the version to be published.

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