▪ Headache Medicine 2022, 13(4):242-248 ▪ p-ISSN 2178-7468, e-ISSN 2763-6178

Headache Medicine

▪ DOI: 10.48208/HeadacheMed.2022.29

Review

Red flags for secondary headaches: challenges in clinical practice

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Edited by:
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Abstract

Introduction
The World Health Organization (WHO) ranks migraine as one of the top 20 causes of impaired healthy life years per year worldwide. Migraine alone is responsible for about 400,000 lost workdays per year per one million inhabitants in developed countries. Headache is probably among the five most important causes of disability worldwide.

Method
This literature review was carried out by searching the Pubmed, Lilacs and Scopus databases, using the following Health Science Descriptors (DeCS) of the Virtual Health Library and in particular the current data collected by the WHO or health entities in the various countries: "secondary headaches" AND "red flags" AND "review". Articles published in Portuguese and English were selected. The eligibility criteria defined for the inclusion of articles were studies that addressed the chosen theme.

Results
The use of "Red Flags" in clinical practice is of considerable relevance. The combination of "Red Flags", anamnesis, physical examination, laboratory, and imaging examination accentuate the probability of predicting the etiology that may underlie the onset of a secondary headache. However, despite this widely useful screening tool, there are still gaps in the prognosis.

Conclusion
Much remains unclear as there is a lack of prospective epidemiological studies. In addition, some "Red Flags" such as pattern change are poorly elucidated. Large-scale studies are needed due to the low incidence of many secondary causes. New patients with headache should be screened using the SNNOOP10 list to increase the likelihood of detecting a secondary cause.

Keywords:
Red flags
Secundary headache
SNNOOP10
Review

Submitted: October 30, 2022
Accepted: December 10, 2022
Published online: December 30, 2022

Introduction

Headache is one of the diseases with the highest reported rates in clinical practice, as well as representing one of the main diseases that lead to the seeking of general practitioners and neurologists in the world. The World Health Organization (WHO) ranks migraine as one of the top 20 causes of impaired healthy life years per year worldwide. Migraine alone is responsible for about 400,000 lost workdays per year per one million inhabitants in developed countries. Headache altogether is probably among the five most important causes of disability worldwide.[1,2]

In the literature, an expressive percentage of individuals with headache complaints is described, in what comprises the daily routine of outpatient care, emergency care, as well as in the units that comprise primary care in Brazil. An epidemiological study revealed that about 95% of women and 91% of men reported having headaches in a period of 12 months, and of these, 18% of women and 15% of men sought medical care due to this condition.[1,2]

Although most headache diagnoses have a benign etiology, its incidence represents a compilation of damages that compromise the quality of life of patients, the execution of their daily activities and family relationships, in addition to generating physical suffering, social, labor, emotional and economic damages, and for students, learning difficulties, with educational failure, school absenteeism and greater vulnerability to comorbidities. In Brazil, headache is one of the most frequent symptoms in the demand for care in primary care.[3]

In the United States of America, the scenario is no different, the impact caused by the prevalence of headaches configures a financial loss in the magnitude of 6 to 18 billion dollars a year. Such values reflect both directly and indirectly the problematic nature of the disease in question.[4]

Methods

This literature review was conducted by searching the PubMed, Lilacs, and Scopus databases, using the following Health Sciences Descriptors (DeCS) of the Virtual Health Library and in particular the current data collected by the WHO or health entities in the various countries: "secondary headaches" AND "red flags" AND "review". Articles published in Portuguese and English were selected. The eligibility criteria defined for the inclusion of articles were studies that addressed the chosen theme.

Results and Discussion

Secondary headaches are caused by conditions that can be demonstrated through clinical and laboratory tests; in these cases, the pain would be the consequence of an aggression to the body of a general or neurological nature, however, it is a symptom linked to a potentially damaging disorder. Secondary headaches can be classified as: post-traumatic headaches, systemic infectious headaches, inflammatory headaches, parasitic headaches, vascular headaches, tumor headaches, metabolic headaches (endocrine disorders), headaches from acute febrile illnesses, headaches related to homeostasis disorders, headaches related to psychiatric disorders, and others. Secondary headaches are directly related to underlying diseases that can have countless etiological backgrounds, such as: infectious, tumoral, traumatic, vascular, metabolic, and others.[5]

Although the diagnosis for secondary headache is less frequent, only 1% of the headaches seen in primary care health centers are caused by underlying intracranial injury such as tumors, meningitis, vascular malformations, subarachnoid hemorrhage, and post traumatic brain injury.[6] When compared to primary headache, a significant portion of patients have lesions concomitant to the headache, that is, 1 in 25 individuals with primary headache identified in the emergency care are of secondary etiology.[7]

After attending to a patient with headache, the physician should be confident to choose between the diagnoses of primary headache or secondary headache. Subsidiary tests should be ordered when the diagnosis of primary headache cannot be confirmed. The diagnostic evaluation usually focuses on the anamnesis. A well-founded history is a key tool for a more reliable diagnosis, as well as the accurate request of complementary exams, when necessary.

In most cases of headache, the clinical history is the main factor for making the correct diagnosis, complemented by the physical examination.[7] The physician must decide what degree of detail is required for its diagnosis and therapy, and it can range from the first to the fourth classificatory digit. The first one gives a superficial notion about the group to which the headache presented by the patient belongs. In what comprises the diagnosis of primary headaches, the evaluation of the symptoms allows the classification of the headache in one or more modalities, in addition to the factor responsible for its physiopathology.[8]

Recognizing and managing "warning signs" in clinical medicine also presents a challenge since all "Red Flags" do not have equal diagnostic power. Some "Red Flags" are general in nature because they have several possible explanations. General "Red Flags" guide physicians to recognize a serious illness even if the exact disease is not known. Unexplained weight loss is one such general "Red Flag". Specific "Red Flags" signal specific disorders and are present in specific anatomical regions.[9]

But all "Red Flags," whether they are highly diagnostic or not, general, or specific, alert us to the possibility of disabilities, disorders, and life-threatening conditions. So, it is important to remember that they only suggest whether the condition is serious enough to be a Red Flag.[10] However, confusion exists because different guidelines have produced a different set of "Red Flags" for the same presentation. Furthermore, guidelines often do not provide information on the diagnostic accuracy of a specific "Red Flag", which limits its value in clinical decision making. Yet, the analysis of "Red Flags" in different clinical evaluations are indispensable as they may indicate an increased likelihood that the patient has a severe pathology. It is imperative to use clinical insight to overcome the deficiencies.[11]

The "Red Flags" terminology was originally developed for the categorization of pain in the regions of the back (acute low back pain) in the early 1980s, and since then numerous efforts have been put into producing increasingly integrated lists. Although the lists encompass a broader set of signs, reading them does not possess supreme diagnostic power. Some signs are potentially indicative of a more severe pathology, while others are of a generalized nature. However, we emphasize the need for its use coupled with clinical judgment to overcome the difficulties associated with the warning signs.[12]

Clinical experience and a large case series of patients with a specific secondary headache form the basis for many "Red Flags". This alone allows the sensitivity of "Red Flags" to be known. The specificity and predictive value of a "Red Flag" are also needed to determine if further testing is required.[13] A prospective study conducted over 5 years at a tertiary headache service included 3,655 patients with non-acute headaches. The authors used "Red Flags" to determine whether a patient should undergo imaging or not. After screening, 530 (14.5%) patients underwent imaging examinations. Only 11 had an abnormality (2.1% of the patients examined and 0.3% of the total study population).[14]

This study revealed that even with the use of red flags, most screenings still did not return with any findings. Thus, an evaluation of the predictive value of "Red Flags" is required. In 2003, the first set of signs encompassing the "Red Flags" for headache was described, the mnemonic SNOOP (systemic signs, presence of focal neurological deficits, papillary edema, seizure, headache that started after age 50, headache of sudden onset or first headache, change in pattern of previous headache or progressive headache (intensity, frequency or duration) or refractory headache) was proposed as an alert detection tool for headache.[17] Afterwards, it went through modifications, such as the insertion of new signs for the possible diagnosis of headache of secondary etiology, named as SNNOOP 10. National and regional guidelines provided more items to screen for possible secondary causes leading to the current SNNOOP10.[15]

Such indicators require a closer clinical look: changes in the headache pattern, progressive headache, headache associated with fever or the presence of systemic symptoms, headache associated with neurological signs, precipitation of the headache (bending over when coughing or sneezing), the appearance of a new headache in an individual over 50 years of age, the appearance of a different pain in the elderly and children, and a change in the pain pattern in individuals diagnosed with cancer.[16]

Fever is a frequent component of hospital visits, and is also a considerable part of a more refined investigation regarding headache of secondary etiology; however, it is important to emphasize that although the "Red Flags" listed above allow a more detailed diagnosis, the investigation of an isolated "Red Flag" needs to be cautious: as with fever, the combination of fever and headache leads the doctor to rule out the possibility of a systemic, neurological, or vascular infection.[17] This is because neuroinfections include meningitis, either bacterial or viral, and the presence of encephalitis and brain abscesses. There is an annual incidence of 4.7 to 7.6 per 100,000 adult populations, but the highest prevalence rates are concentrated in children under 14 years of age.[18]

In this light, although fever represents an important sign, its investigation needs more attention, since its presence is not usually indicative of the need for a more detailed analysis. Such observation was made by Limper and collaborators[19] who found that in a group of 213 patients with fever and pneumonia, only one patient was diagnosed positive for meningitis.[19] The literature highlights numerous investigations of individuals with meningitis who jointly presented fever, nuchal rigidity in addition to reduced consciousness.[20] Despite these findings, the presentation

of the above triad is not characterized as a rule, because this compilation of symptoms is not typical of episodes of neuroinflammation.[20]

Among the long list of "Red Flags", some are more prevalent, such as having experienced the worst headache in a lifetime. Therefore, the study conducted by Lamont[21] identified that 28.8% of patients reported having the worst headache ever experienced, and among the "Red Flags" investigated, three were prevalent, namely: paralysis, papilledema, and a cluster of symptoms related to confusion, sleepiness, and memory loss.[21] The "Red Flags" listed were considered by the authors to be important factors in performing an imaging exam.

Studies conducted by Garcia-Azorín and collaborators[22] demonstrated the presence of a set of "Red Flags" in 76% of the patients who were positive for Covid-19 and highlighted the presence of systemic symptoms such as fever and the presence of precipitation by sneezing or coughing. Indicating that the identification of these signs is a differential for making fundamental decisions to ensure the well-being of the patient. Another important finding also related to Covid-19 indicated an association between the effects of the vaccine and the delayed onset of headache, which may be associated with the diagnosis of cerebral venous thrombosis. Being promising indications for a new warning sign, it may constitute a "Red Flag" for cerebral venous thrombosis, indicating that patients with recent onset of headache after vaccination should undergo a clinical investigation.[21]

However, despite the compilation of warning signs, the use of neuroimaging in medical routine is still pertinent and has increased considerably, with a significant increase in the last decades being prominent in the United States.[22] Linked to this is the fact that patients with chronic migraine are usually submitted to neuroimaging. However, such a practice goes against current guidelines and has the direct consequences of exposing the patient to radiation(if investigated by computed tomography of the skull), obtaining false-positive results, and the high costs involved.[22]

In what corresponds to the evaluation of the patient with a headache, the analysis of the entire patient history guided by the evaluation of the "Red Flags" directs the identification of abnormalities that may represent risks to the patient's health. Therefore, patients who present with headaches and one or more "Red Flags" should be referred for tests that include: neuroimaging, cerebrospinal fluid, and other tests that the doctor deems necessary. The treatment and prognosis are subject to the pathophysiology of the headache. However, the finding in a short period of time is essential to mitigate an unfavorable outcome that can be fatal in some cases.

The use of "Red Flags" in clinical practice is of considerable relevance. The combination of "Red Flags", anamnesis, and physical, laboratory, and imaging examination accentuate the likelihood of predicting the etiology that may underlie the onset of a secondary headache. Some epidemiological studies have shown promise in clarifying underlying diseases and the beginning of headaches. However, despite this widely useful screening tool, there are still gaps in what concerns prognosis.

Another point of concern lies in the continuity of entrenched practices that need modification since several different guidelines and scientific findings demonstrate the lack of cost-effectiveness of investigations and patients with primary headache complaints. Finally, we highlight the need for regulatory and legislative support to promote the encouragement of best practices without fear of financial penalties to practitioners regarding the use of "Red Flags", In addition, there is a need for more epidemiological studies on this theme. Its consequences and social impact must be considered in the planning of health actions and its problem must be part of the debate agenda of primary care teams, with a broad discussion between professionals and patients to adopt more efficient and accessible conduct, without the tendency to inadvertently use heavier technologies that are not only ineffective but also costly to the health system.

Conclusion

A "Red Flag" approximation of sensitivity is often possible, while specificity is more difficult to assess because most studies on the occurrence of clinical symptoms are based on retrospective studies of patients with secondary disease known as a headache disorder. New patients with headache should be screened using the SNNOOP10, or similar warning signs,[23-44] to increase the likelihood of detecting a secondary cause.[43-44] A combination of "Red Flags" can increase the chances of predicting the underlying etiology of a secondary headache.

Much remains unclear as there is a lack of prospective epidemiological studies. In addition, some "Red Flags" such as pattern change is poorly elucidated. Large-scale studies are needed due to the low incidence of many secondary causes. A validated screening tool for headaches using

"Red Flags" would be helpful, such as assessing mild TBI, to minimize the amount of unnecessary testing and patient anxiety. Ultimately, validating a screening tool will lead to greater awareness of secondary headaches.

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Funding
This study was not financed.

Conflicts of interest
The author declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

Authors contribution: MCML, GSM, Conceptualization, Investigation, Writing - Original Draft, MMV, Writing - Review & Editing

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