INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES
(p-ISSN: 2348-5213: e-ISSN: 2348-5221)
www.ijcrcps.com
DOI: 10.22192/ijcrcps Coden: IJCROO(USA) Volume 5, Issue 12 - 2018

Research Article

DOI: http://dx.doi.org/10.22192/ijcrcps.2018.05.12.003

Frequency of Primary Headache in Iranian Patients with Multiple Sclerosis: A systematic review and meta analysis

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Abstract

Objective: the aim of this systematic review and meta-analysis was to evaluate the Frequency of Primary Headache in Iranian Patients with Multiple Sclerosis
Method: Two separate researchers conducted studies until November 2018 at international (PubMed, Google Scholar, and WOS) and national (SID and Magiran) databases in English and Persian, without any time limit. The key words used in the research strategy included: primary headache , multiple sclerosis , prevalence , frequency and Iran, which were combined with Boolean agents such as AND, OR, NOT. The final data extracted using the STAT 14.0 statistical software.
Results: all of the 3 research studies were included in the final analysis context.. The prevalence of primary headache in Iranian MS patients was 60.5%(95% CI :55.5% , 63.5; I^2 = 78.3%).
Discussion and conclusion: According to the present study, headache is common in MS patients and is seen in more than half of these subjects; thus, clinical evaluation is recommended in all patients with MS, because their combined association has a significant effect on the quality of life and performance of the patients; it is also, recommended to conduct more studies with larger sample sizes in order to identify the relationship between headache and MS and their accompanying mechanisms

Keywords: primary headache , multiple sclerosis , prevalence

Introduction

Multiple Sclerosis is one of the most common autoimmune diseases that affects the central nervous system; it is characterized by inflammation, malignant myelin and scar (1), and it causes sensory impairment, weakness, muscle cramps, visual impairment, cognitive impairment, fatigue, limb shaft, urinary and fecal dysfunction, sexual dysfunction, imbalance, forgetfulness, hearing impairment, blurred vision, dyspnea and speech impairment in patients. (2)

Clinical symptoms are commonly seen in young ages and in different parts of the central nervous system at different times. Common clinical symptoms include visual impairment, walking disorders, limb weakness, and imbalance; however, in addition to the above symptoms, a variety of other complications, including pain, occur during the course of the disease(3). Despite the fact that pain is not the main symptom of MS, many MS patients suffer from various types of pain, including headache; the results of a study conducted by Clifford indicated that 28.88% of patients with MS experience pain in different parts of their body(5).Headache is one of the most common causes for visiting physician, and about 40% of individuals experience severe headaches during their lives(6). Initial headaches are disorders that cause headaches and other symptoms in the absence of any external agent, the most common types of which include migraine, tension type headache and cluster headache(7). The most important form of debilitating and recurrent headache is migraine, which causes

significant decrease in quality of life in many patients; despite being the most common type of headache, tension headache rarely makes it difficult for the person to develop and usually improves with drug use(8).Pain in these patients can have central or environmental causes; it, even, sometimes, is a sign of the early symptoms of the disease or an indication of exacerbation such as neuralgia,lhermitteor tonic spasm(9). Headache types are common in MS patients and can be due to the disease itself or complication of drug use or depression caused by the disease and can affect the diagnosis, treatment and quality of life of patients(9,10).According to various reports about types of headaches in patients with MS and considering that there are lesions in the cerebral MRI of patients with migraine that may be misleading with MS lesions,(11,12) and given the increasing trend of MS among Iranian subjects, the present study was conducted to determine the prevalence of headache among MS patients in Iran.

Materials and Methods

The present systematic investigation applies developed methods that are consistent with the accurate instructions in the PRISMA check list.

Inclusion and exclusion criteria

Observational studies, including posting to editors, publications, poor quality articles (based on the Hoy's tool) and studies on adult subjects were only excluded from the study. Only articles in English and Persian are included.

Sampling methods and sample size

All observational studies with any sampling and statistical surveys were included in the present systematic study.

Research strategy

Two separate researchers conducted studies until November 2018 at international (PubMed, Google Scholar, and WOS) and national (SID and Magiran) databases in English and Persian, without any time limit. We examined a list of available articles sources for further related article searches. Specific research strategies have been developed using the MESH vocabulary explorer and free vocabularies, according to the PRESS standard, by a Health scientist librarian specializing in research on systematic review. We used the MEDLINE research strategy to investigate other databases. The key words used in the research strategy included: primary headache ,multiple sclerosis , prevalence , frequency and Iran, which were combined with Boolean agents such as AND, OR, NOT.

Selection of research and data extraction:

Two separate researchers examined the titles and abstracts by considering qualifying criteria. After removing the repetitive research, the full text of the research was examined depending on the qualifying criteria and the required data was extracted.

To answer questions regarding qualifications, additional research information was obtained from the authors in case it is required. The general information (first author, province, and year of publication), research characteristics (sampling method, research design, location, sample size and bias risk), and the measurement of results (frequency of primary headache) were also collected.

Quality assessment and abstraction:

Hoy's et al. tool was used to assess the methodological quality and the risk of getting away from the truth (bias) for each one of the observational studies. This tool evaluates 10 items for assessing the quality of studies in two dimensions such as foreign (items 1-4, target population, sampling frame, sampling method and the minimum deviation from response) and domestic credits (the issues 5-9 of the data collection method, case definition, research tool, data collection mode were assessed while the issue 10 of the bias evaluation was related to data analysis). The higher index indicated that the bias is likely to reduce and the lower index indicated the risk of more bias. The separate bias risk was investigated by two researchers. Consensus was used to solve the disagreements.

Data combination:

The final data extracted using the STAT 14.0 statistical software, including studies combined with stock diagram and the primary headache frequency, were assessed with random effect of the model.

Results

In the initial search conducted in different databases, 430 articles were reviewed. From among these articles, as many as 401 were considered as duplicate in the screening process of titles and abstracts. As many as 18 articles were excluded for having irrelevant titles. From among the 11 remaining articles, 3 articles met the eligibility criteria. From the 8 articles that were excluded, 3 articles were reviews, 2 articles were letters to editor, 1 article did not have a full text, and 2 articles had poor quality that could not be included in the present study (Figure 1).

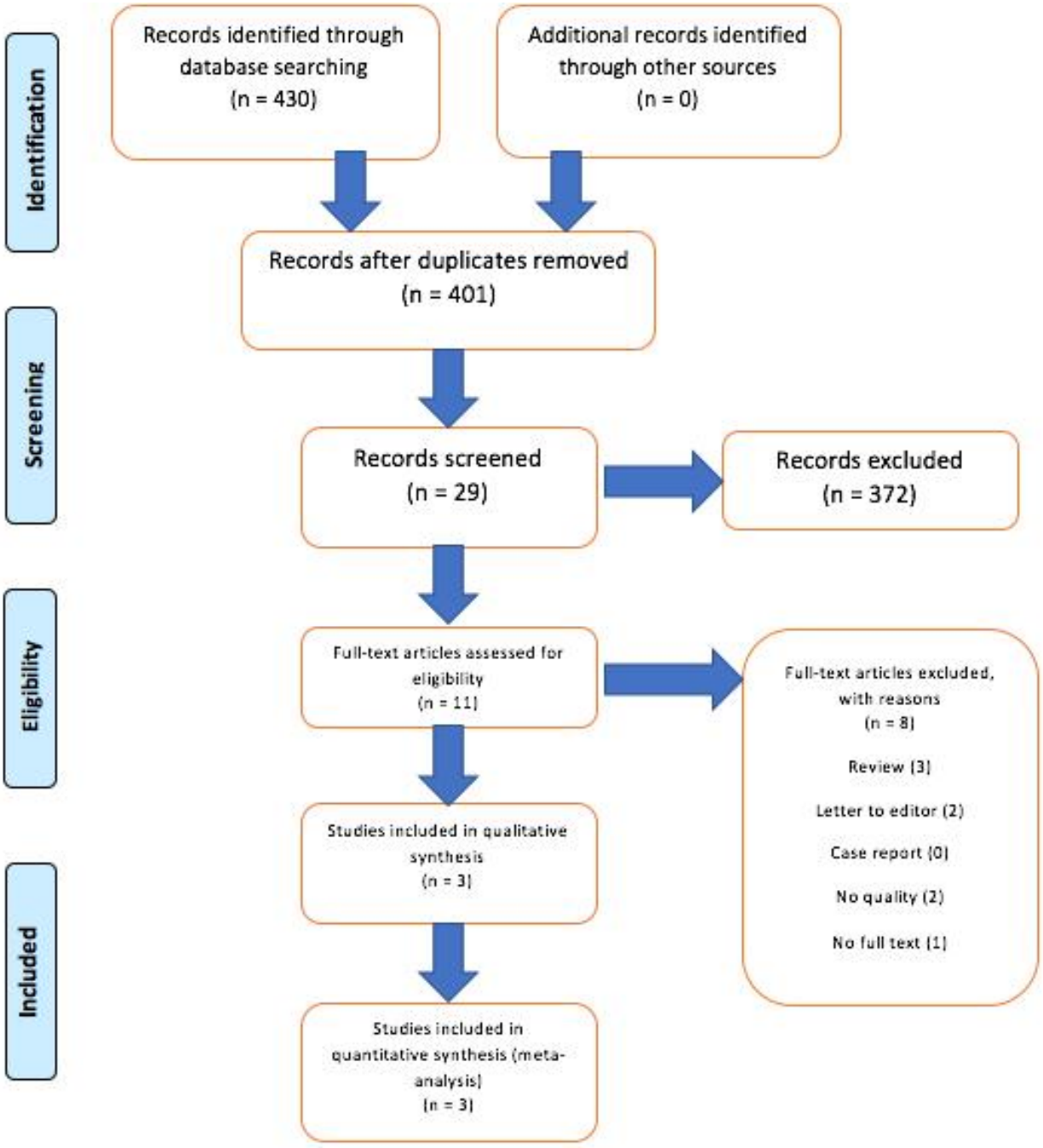

Fig 1. Study selection process

Research characteristics

These 3studies were conducted on 350 Iranian MS patients. all of the 3 studies, provided cross-sectional data.. Out of the 3 studies, one was from Qazvin province, one from Mashhad, and one from Isfahan province. The most commonly used sampling method was convenience (easiness), (n = 3). All studies had a low bias risk. The most common place to conduct the studies was in the hospital (n = 3). all of the 3 research studies were included in the final analysis context. Theprevalence of primary headache in Iranian MS patients was 60.5%(95% CI :55.5% ,65.5%; I^2 = 78.3%) (Table . 1).

Table 1. Studies included in the systematic review

First Author	year	Province	Sample size	Female to male	Risk of bias
Ashtari[16]	2009	Esfehan	100	1.38	Low
Mozhdehpanah[17]	2017	Qazvin	150	4.35	Low
Alehashemi[18]	2015	Mashhad	100	3	Low

Frequency of Primary Headache in Iranian Patients with Multiple Sclerosis

3 studies conducted on 350 Iranian MS patients were included in the meta-analysis. In Iranian MS patients, the overall prevalence of primary headache in 350 MS patients was 60.5%(95% CI :55.5% ,63.5; I^2 = 78.3%) [Table 2].

Table 2:**Frequency of Primary Headache in Iranian Patients with Multiple Sclerosis**

ID	First Author	Year	Province	ES	95% CI for ES	% Wight
1	Ashtari	2009	0.67	0.67	0.578	0.762
2	Mozhdehpanah	2017	0.64	0.64	0.564	0.716
3	Alehashemi	2015	0.48	0.48	0.384	0.576
Sub-total Random pooled ES	-------	------	------	0.605	0.555	0.635

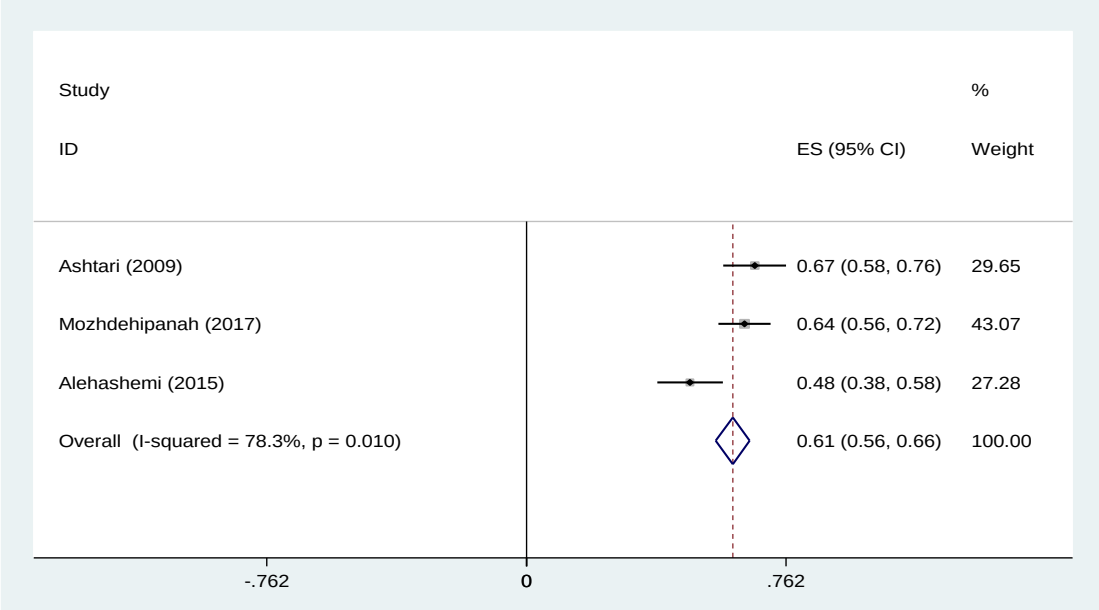

Fig. 2 :The Frequency of Primary Headache in Iranian Patients with Multiple Sclerosis and its 95% interval for the studied cases according to the year and the city where the study was conducted based on the model of the random effects model. The midpoint of each section of the line estimates the% value and the length of the lines showing the 95% confidence interval in each study. The oval sign shows Frequency of Primary Headache in Iranian Patients with Multiple Sclerosis for all studies.

Discussion

According to the results of the present study, headache is quite common among MS patients and the majority of them experiencing a variety of headaches. The most common type of headache in these patients is tension headache and migraine; migraine was reported to be more frequent and observed in 23% of patients(13,14). 55.2% of the patients had headaches during the attack, and 5.4% experienced headache only during MS attacks(15). Therefore, the occurrence of headache in patients with MS can be important. According to the present study, headache is common in MS patients and is seen in more than half of these subjects; thus, clinical evaluation is recommended in all patients with MS, because their combined association has a significant effect on the quality of life and performance of the patients; it is also, recommended to conduct more studies with larger sample sizes in order to identify the relationship between headache and MS and their accompanying mechanisms. Concurrent attention to these two diseases can play an important role in prescribing medication and other common treatments for two diseases. Additional studies on more patients are necessary to confirm the findings of the present research.

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Quick Response Code

DOI: 10.22192/ijcrcps.2018.05.12.003

How to cite this article:
Khosro Jamebozorgi, Hosein Pormasoumi. (2018). Frequency of Primary Headache in Iranian Patients with Multiple Sclerosis: A systematic review and meta analysis. Int. J. Curr. Res. Chem. Pharm. Sci. 5(12): 13-18.
DOI: http://dx.doi.org/10.22192/ijcrcps.2018.05.12.003