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Review

Fibromyalgia in patients with migraine: A literature review in the last 20 years

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Abstract

Introduction

Possibly fibromyalgia and migraine share similar pathophysiological mechanisms, generating an imbalance of neurotransmitters involved in pain modulation, with increased neuronal excitability. The association between these two conditions is frequent, increasing the disability of both.

Objectives

We aimed to review articles published in the last 20 years about the presence of fibromyalgia in patients with migraine and to analyze the quality of life of these patients.

Methods

Based on a literature search in the major medical databases and using the descriptors "migraine" and "fibromyalgia" we include articles published between 2001 and 2021. We found 387 articles, but only five met the inclusion criteria.

Results

In five articles analyzed, 429 patients with migraine were found, in which fibromyalgia was present in 31.5% of them, predominantly in women ($p<0.0001$). In this association, there was a higher risk for depression and worse quality of life.

Conclusions

The association of fibromyalgia in patients with migraine is frequent, increasing the disability of these two diseases and generating great social impact. Knowledge of this association and the management of its consequences are necessary in medical practice.

Keywords:
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Introduction

Fibromyalgia is a chronic condition of diffuse musculoskeletal pain, accompanied by a series of nonspecific symptoms, including sleep disturbances and affective dysfunction, in the absence of any objective organic cause.[1] It affects, on average, 2% to 3.6% of the world population.[2-4]

Its pathophysiology is not completely known yet. However, a genetic predisposition was found in the imbalance of neurotransmitters involved in pain modulation, with increased neuronal excitability. Clinical expression is diffusely increased pain sensitivity,[5] associated with depression and behavioral abnormalities.[6]

Diagnostic criteria for fibromyalgia were established by the American College of Rheumatology, 1990. It is necessary the presence of diffuse musculoskeletal pain for at least three months, and the positivity of at least 11 of the 18 predetermined sites of the body, called tender points.[7] According to the current criteria, other variables such as sleep and mood disorders, headache, and visceral pain must be considered.[1,8]

The association of fibromyalgia with migraine is frequent, increasing the incapacity of both.[9-11] Possibly, there is a common pathophysiological mechanism, with central nervous system dysfunction, which may benefit from the same treatment.[4,12]

It is estimated that the occurrence of fibromyalgia in patients with migraine varies from 22.2% to 45.1%.[4,9,13-15] On the other hand, patients with fibromyalgia have a high prevalence of migraine, around 55.8%.[16,17] The reasons for this association are still reasons for intense investigation.[1]

Despite its relevance, the association between migraine and fibromyalgia is still poorly studied. There is a scarcity of studies, despite the high prevalence of this co-morbidity. Based on this, the authors decided to review the articles on the association between migraine and fibromyalgia that have been published in the last 20 years.

Methods

This study was an integrative and retrospective review of the articles on fibromyalgia in patients with migraine published in the last 20 years. The research was performed in the online databases LiLacs, SciELO and PubMed, from September to November 2021, using the descriptors "migraine" and "fibromyalgia".

Articles published from 2001 to 2021 that addressed the discussion of migraine and fibromyalgia and written only in English were included. Editorials, comments, letter to the editor, articles that were not fully available or those who lacked accurate information were excluded. To ensure the validity of these articles, the selected studies were analyzed in detail regarding the demographic and clinical characteristics and quality of life of these patients.

Of the 387 articles found, repeated articles or articles that did not address the relationship between migraine and fibromyalgia were eliminated and only 90 remained and were analyzed. After reading the abstracts and selecting those that met the inclusion criteria, five articles remained (case series), totaling 429 patients.

Data were analyzed based on demographic and clinical features. They were presented as an arithmetic mean with the standard deviation (SD), or as percentages. The percentage was always related to the total number of patients whose information was available for the specific issue. All collected data were organized in a database. The BioEstat version 5.0 for statistical analysis was used.

Results

A total of 429 patients (68.3% women and 31.7% men) were diagnosed with migraine and analyzed in this review, in which fibromyalgia comorbidity was present in 31.5% (135/429) and absent in 68.5% (294/429). Regarding gender, fibromyalgia predominated in women ($p<0.0001$), as shown in Table 1.

Table 1. Distribution of 429 migraine patients with and without fibromyalgia, according to age and sex

Authors, citation	Migraine patients with FM (n=135)			Migraine patients without FM (n=294)		
	n (%)	Sex (M/F)	Average age (years, min-max or SD)	n (%)	Sex (M/F)	Average age (years, min-max or SD)
Küçükşen et al.[4]	37 (31.4)	7/30	37 (20–64)	81 (68.6)	22/59	36 (16–66)
De Tommaso et al.[14]	23 (45.1)	3/20	40	28 (54.9)	9/19	36
Beyazal et al.[13]	28 (32.6)	1/27	38.6 ± 9.5	58 (67.4)	16/42	33.9 ± 10.3
Onder et al.[9]	31 (30.4)	1/30	36.9 ± 10.0	71 (69.6)	57/14	32.5 ± 9.2
Onder et al.[9]	16 (22.2)	0/16	43.4 ± 11.4	56 (77.8)	20/36	43.6 ± 12.5

Note: FM – fibromyalgia

Quality of life in migraine patients with and without fibromyalgia was assessed by MIDAS (Migraine Disability Assessment Scale), HIT-6 (Headache Impact Test) and FIQ (Fibromyalgia Impact Questionnaire) scores, as shown in Table 2.

Table 2. Quality of life among migraine patients with and without fibromyalgia, according to MIDAS, HIT-6 and FIQ scores

Authors, citation	MIDAS (mean±SD or range)	HIT-6 (mean±SD or range)	FIQ (mean ± SD)
Küçükşen et al.[4]			
migraine patients without FM	25 (3–110)	62 (42–71)	
migraine patients with FM	26 (4–105)	64 (48–78)	53.2±12.8
p value	0.150	0.003	
De Tommaso et al.[14]			-
migraine patients without FM	38.0±38.95	-	44.53±16.44
migraine patients with FM	71.35±63.9	-	
p value	0.026	-	-
Beyazal et al.[13]			
migraine patients without FM	23.3 ± 22.6	58.4±14.5	24.1±11.2
migraine patients with FM	27.6 ± 18.9	62.8±7.1	66.5±10.3
p value	0.390	0.481	<0.001
Onder et al.[9]			
migraine patients without FM	17.3±25.8	59.9±6.3	-
migraine patients with FM	36.2±40.0	63.3±5.2	-
p value	0.002	0.041	-
Ifergane et al.[15]			
migraine patients without FM	15.6±21.1 (0–95)	48.4±9.5 (30–66)	-
migraine patients with FM	17.8±23.4 (0–90)	49.2±9.9 (30–64)	-
p value	NS	NS	-

Note: MIDAS – Migraine Disability Assessment Scale; HIT-6 – Headache Impact Test; FIQ – Fibromyalgia Impact Questionnaire; SD – standard deviation; FM – fibromyalgia.

Discussion

Migraine and fibromyalgia are two very prevalent diseases that affect, respectively, 15%18 and 2% to 3.6%[2-4] of the world population. The association between them is frequent, causing mutual aggravation, making the diagnosis difficult and influencing the prognosis.[1,9-11,19] Despite this high degree of co-morbidity, there are still few epidemiological studies.[20]

Fibromyalgia occurs in patients with migraine, just as migraine also occurs in patients with fibromyalgia, characterizing a bidirectional association.[10,16,17,21] Therefore, this association was called fibromigraine.16 However, in this review, we only investigated the presence of fibromyalgia in migraine patients.

In our review, the occurrence of fibromyalgia in migraine patients ranged from 22.2% to 45.1%.4,9,[13-15] Possibly, there is a common pathophysiological mechanism, with central nervous system dysfunction, which may benefit from the same treatment.[4,12,16] These associations may involve painful conditions at a visceral, musculoskeletal, or craniofacial level.[22]

In the pathophysiology of migraine, there is a vascular component mediated by inflammatory cytokines and neuropeptides, including calcitonin gene-related peptide (CGRP) and substance P and central mechanisms of hyperexcitability.[1] On the other hand, there is evidence of central sensitization in chronic migraine, leading to decreased pain thresholds against different types of stimuli at the somatic level.[9,12] These pathophysiological mechanisms are shared with fibromyalgia, in which generalized musculoskeletal pain activates local nociceptors transmitting pain impulses through the superior cervical spinal nerves to the caudal trigeminal nucleus and inducing a migraine attack.[10]

We found that women with migraine had more fibromyalgia than men (41.2% versus 8.8%). Studies in the general population have shown that women tend to be more affected than men, in a ratio of 3:1,[11,23,24] but there is no evidence for the role of sex hormones in fibromyalgia. However, there are studies suggesting that estrogen and progesterone exert antinociceptive and anti-inflammatory effects through the regulation of the serotonergic pathway.[6]

In assessing the quality of life of patients with migraine and fibromigraine, we analyzed two scores: Migraine Disability Assessment Scale (MIDAS) and Headache Impact Test (HIT-6), both to quantify headache-related disability,[11,25,26] in which we identified higher scores in fibromigraine.[4,9,14] Fibromyalgia Impact Questionnaire (FIQ) was used to assess health status, progress, and outcomes in patients with fibromigraine[27] who received high scores.[4,13,14]

It was found that the impact on the quality of life of patients with fibromigraine is great, with a tendency to have more intense headache attacks (62.2% *versus* 42%, p=0.017), a greater risk of depression (75% *versus* 62%,) and anxiety (86% *versus* 63%).[4] In addition, patients with fibromigraine have a greater number of medical and psychiatric comorbidities than those with fibromyalgia alone.[17]

Conclusion

The association of fibromyalgia in patients with migraine is frequent, increasing the disability of these two diseases and generating great social impact. Knowledge of this association and the management of its consequences are necessary in medical practice.

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References

1. Affaitati G, Costantini R, Tana C, Cipollone F and Giamberardino MA. **Co-occurrence of pain syndromes**. *J Neural Transm (Vienna)* 2020;127(4):625-646 Doi:10.1007/s00702-019-02107-8
2. Cabo-Meseguer A, Cerdá-Olmedo G and Trillo-Mata JL. **Fibromyalgia: Prevalence, epidemiologic profiles and economic costs.** *Med Clin (Barc)* 2017;149(10):441-448 Doi:10.1016/j.medcli.2017.06.008
3. Heidari F, Afshari M and Moosazadeh M. **Prevalence of fibromyalgia in general population and patients, a systematic review and meta-analysis**. *Rheumatol Int* 2017;37(9):1527-1539 Doi:10.1007/s00296-017-3725-2
4. Küçükşen S, Genç E, Yılmaz H, Sallı A, Gezer İ A, Karahan AY, . . . Uğurlu H. T**he prevalence of fibromyalgia and its relation with headache characteristics in episodic migraine**. *Clin Rheumatol* 2013;32(7):983-990 Doi:10.1007/s10067-013-2218-2
5. Grayston R, Czanner G, Elhadd K, Goebel A, Frank B, Üçeyler N, . . . Alam U. **A systematic review and meta-analysis of the prevalence of small fiber pathology in fibromyalgia: Implications for a new paradigm in fibromyalgia etiopathogenesis**. *Semin Arthritis Rheum* 2019;48(5):933-940 Doi:10.1016/j.semarthrit.2018.08.003
6. Singh L, Kaur A, Bhatti MS and Bhatti R. **Possible Molecular Mediators Involved and Mechanistic Insight into Fibromyalgia and Associated Co-morbidities**. *Neurochem Res* 2019;44(7):1517-1532 Doi:10.1007/s11064-019-02805-5
7. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, . . . et al. **The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee**. *Arthritis Rheum* 1990;33(2):160-172 Doi:10.1002/art.1780330203
8. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, . . . Walitt B. **2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria**. *Semin Arthritis Rheum* 2016;46(3):319-329 Doi:10.1016/j.semarthrit.2016.08.012
9. Onder H, Hamamci M, Alpua M and Ulusoy EK. **Comorbid fibromyalgia in migraine patients: clinical significance and impact on daily life**. *Neurol Res* 2019;41(10):909-915 Doi:10.1080/01616412.2019.1630164
10. Penn IW, Chuang E, Chuang TY, Lin CL and Kao CH. **Bidirectional association between migraine and fibromyalgia: retrospective cohort analyses of two populations**. *BMJ Open* 2019;9(4):e026581 Doi:10.1136/bmjopen-2018-026581
11. Whealy M, Nanda S, Vincent A, Mandrekar J and Cutrer FM. **Fibromyalgia in migraine: a retrospective cohort study**. *J Headache Pain* 2018;19(1):61 Doi:10.1186/s10194-018-0892-9
12. Yilmaz V, Aras B, Erturk FA, Cakcı FA and Umay E. **Migraine in patients with fibromyalgia and outcomes of greater occipital nerve blockage**. *Clin Neurol Neurosurg* 2019;181:54-57 Doi:10.1016/j.clineuro.2019.04.004
13. Beyazal MS, Tüfekçi A, Kırbaş S and Topaloğlu MS. T**he Impact of Fibromyalgia on Disability, Anxiety, Depression, Sleep Disturbance, and Quality of Life in Patients with Migraine**. *Noro Psikiyatr Ars* 2018;55(2):140-145 Doi:10.5152/npa.2016.12691
14. Tommaso M, Federici A, Loiacono A, Delussi M and Todarello O. **Personality profiles and coping styles in migraine patients with fibromyalgia comorbidity**. *Compr Psychiatry* 2014;55(1):80-86 Doi:10.1016/j.comppsych.2013.08.006
15. Ifergane G, Buskila D, Simiseshvely N, Zeev K and Cohen H. **Prevalence of fibromyalgia syndrome in migraine patients**. *Cephalalgia* 2006;26(4):451-456 Doi:10.1111/j.1468-2982.2005.01060.x
16. Silva LC, Oliveira DA, Martins HAL, Medeiros FL, Araújo LCL, Serva WAD, . . . Valença MM. **Fibromigrânea: uma nova denominação para uma velha doença?** *Headache Medicine* 2011;2(3):89-95 Doi:10.48208/HeadacheMed.2011.19
17. Vij B, Whipple MO, Tepper SJ, Mohabbat AB, Stillman M and Vincent A. **Frequency of Migraine Headaches in Patients With Fibromyalgia**. *Headache* 2015;55(6):860-865 Doi:10.1111/head.12590
18. **Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013**. *Lancet* 2015;386(9995):743-

800 Doi:10.1016/s0140-6736(15)60692-4
19. Cho SJ, Sohn JH, Bae JS and Chu MK. **Fibromyalgia Among Patients With Chronic Migraine and Chronic Tension-Type Headache: A Multicenter Prospective Cross-Sectional Study**. *Headache* 2017;57(10):1583-1592 Doi:10.1111/head.13191
20. Stuginski-Barbosa J, Dach F and Speciali JG. **Relação entre cefaléia primária e fibromialgia: revisão de literatura**. *Revista Brasileira de Reumatologia* 2007;47:114-120
21. Centonze V, Bassi A, Cassiano MA, Munno I, Dalfino L and Causarano V. **Migraine, daily chronic headache and fibromyalgia in the same patient: an evolutive "continuum" of non organic chronic pain? About 100 clinical cases**. *Neurol Sci* 2004;25 Suppl 3:S291-292 Doi:10.1007/s10072-004-0314-4
22. Giamberardino MA, Affaitati G, Martelletti P, Tana C, Negro A, Lapenna D, . . . Costantini R. **Impact of migraine on fibromyalgia symptoms**. *Headache Pain* 2015;17:28 Doi:10.1186/s10194-016-0619-8
23. Vetvik KG and MacGregor EA. **Sex differences in the epidemiology, clinical features, and pathophysiology of migraine**. *Lancet Neurol* 2017;16(1):76-87 Doi:10.1016/s1474-4422(16)30293-9
24. Steiner TJ, Stovner LJ, Katsarava Z, Lainez JM, Lampl C, Lantéri-Minet M, . . . Andrée C. **The impact of headache in Europe: principal results of the Eurolight project**. *J Headache Pain* 2014;15(1):31 Doi:10.1186/1129-2377-15-31
25. Kosinski M, Bayliss MS, Bjorner JB, Ware JE, Jr., Garber WH, Batenhorst A, . . . Tepper S. **A six-item short-form survey for measuring headache impact: the HIT-6**. *Qual Life Res* 2003;12(8):963-974 Doi:10.1023/a:1026119331193
26. Stewart WF, Lipton RB, Dowson AJ and Sawyer J. **Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability**. *Neurology* 2001;56(6 Suppl 1):S20-28 Doi:10.1212/wnl.56.suppl_1.s20
27. Burckhardt CS, Clark SR and Bennett RM. **The fibromyalgia impact questionnaire: development and validation**. *J Rheumatol* 1991;18(5):728-733