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Association between trigeminal neuralgia and multiple sclerosis in Iranian patients: A systematic Review and meta-analysis

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Abstract

Introduction:

Multiple sclerosis (MS) is a chronic neuro-inflammatory disease of central nervous system (CNS) which is characterized by variable evolution and different clinical manifestations. Although pain is one of the most common problems of MS patients, the presence of trigeminal neuralgia (TN) in a patient's life-span is rare. Considering that trigeminal neuralgia is one of the symptoms of the onset of MS, this systematic review and meta-analysis was conducted to determine the prevalence of Trigeminal neuralgia in Iranian MS patients.

Methods:

The methods used for this systematic review were based on the "Cochrane Systematic Study Booklet" and "Appropriate Items for Systematic review and Meta-Analysis Study (PRISMA)" tool. Observational studies conducted on general population have been added and studies conducted on specific population have been removed. Results are summarized as reported in the research. The minimum sample size was 25 patients in each study. To find references, the international Databases (MEDLINE PubMed interface), Google Scholar, and Web of Science) and domestic databases (SIDs and Magiran) and journals were searched; unlimited searching, in terms of both setting and language, was done until June 30, 2018.

Results:

In the initial search on various databases, a total of 461 articles were reviewed, 432 of which turned out to be repetitive during screening process of title and abstract. 19 articles were removed due to unrelated title; out of the remaining 10 articles, 5 articles met the inclusion criteria. Based on the results of random effects model, the Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients in 2273 patients was %05.8 (95% confidence interval [CI]: 4.9, 6.7, $I^2 = 88\%$).

Conclusion:

The prevalence of trigeminal neuralgia in patients with multiple sclerosis turned out to be 5.8% in the present study. This issue highlights the need for physicians to be aware of the causes of facial atypical pain, including triple-nerve pain, especially in patients under 40 years of age. Adequate knowledge and timely diagnosis of trigeminal neuralgia, as the first symptom of MS disease, can help physicians diagnose the disease timely; in case of positive diagnosis, the physicians can start treatments rapidly, avoiding the use of inappropriate and unnecessary therapies.

Keywords: Neuralgia, Trigeminal nerve, trigeminal neuralgia, Facial pain, MS, Multiple sclerosis

Introduction

Generally speaking, the term neuralgia refers to severe and regular paroxysmal pains, which are often limited to the branches of the head and neck nerves(1-3). MS is one of the causes of symptomatic neuralgia, the first symptom of which may appear as pain(4). However, there are usually other symptoms and sensory motor disorders associated with it(5). Multiple sclerosis can be one of the most common diseases of the central nervous system in humans (6). This neurodegenerative disease, which often affects young adults and is more common in women in comparison with men, is associated with the destruction of myelin nerves; it usually develops during the fourth decade of life, but it might also be witnessed at other stages of life(7). The main cause of MS is unknown; however, the certain point is that environmental, genetic and autoimmune factors play an important role, and parts of northern Europe and the south Canada, the north of the United States, and southern Australia are considered as high risk areas(8). The disease is characterized by multiple lesions in terms of time and place; the occurrence of symptoms is reversible; i.e(9). a neurological symptom improved after some time, but reoccurs later multiplied with other disorders(10). Although the healing can be complete, the nervous system may gradually disable the patient(11-13). Common symptoms that result from MS attack include visual impairment, muscle imbalance, bladder dysfunction, imbalance, and vertigo(14). Trigeminal neuralgia is the most commonly diagnosed neurologic disease affecting people over the age of 50 years(15). The main cause of neuralgia remains controversial, but about 10% of the cases involve certain pathogenic diseases such as cerebellum, MS, or vascular malformations(16). The remaining percentages cover idiopathic neuralgia cases; trigeminal nerve begins suddenly with the nature of an electrical shock(17). This may start with touching the chin, brushing or chewing(18). This pain is usually very severe, its time is short and within a few seconds, but it can be repeated many times per day(19). Considering that trigeminal neuralgia is one of the symptoms of the onset of MS, this systematic and meta-analytic

review was conducted to determine the prevalence of Trigeminal neuralgia in Iranian MS patients.

Methods

Eligibility criteria

The methods used for this systematic review were based on the "Cochrane Systematic Study Booklet" and "Appropriate Items for Systematic and Meta-Analysis Study (PRISMA)" tool. Observational studies conducted on general population have been added and studies conducted on specific population have been removed. Results are summarized as reported in the research. The minimum sample size was 25 patients in each study. The target population covers the total population of Multiple sclerosis Patients who entered the study. Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients was calculated in this study.

Searching strategies and databases

The review of references and resources was done using the Medical Subject Headings (MeSH) and keywords related to the source of information on Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients. To find references, the international Databases (MEDLINE PubMed interface), Google Scholar, and Web of Science) and domestic databases (SIDs and Magiran) and journals were searched; unlimited searching, in terms of both setting and language, was done until June 30, 2018. PRESS standard and the Health Sciences Librarian were used for designing the strategy.

MEDLINE application was used to search other databases. In addition, PROSPERO was used to provide a systematic search that was completed recently. To search for headlines and abstracts, boolean (AND, OR, NOT), mesh, coordinate {truncation} * and related words were used; following keywords were used to provide a comprehensive context: Neuralgia, Trigeminal nerve, Facial pain , MS ,Multiple sclerosis.

Research selection and data extraction

According to the research protocol, two researchers observed the titles and abstracts separately according to the eligibility criteria; in the next step, after the removal of repeated studies, the full text of the paper was studied based on the eligibility criteria and the required information was extracted. Consensus method was used to solve the disagreements between two researchers. The extracted data included the general information (corresponding author, year and place), characteristics of the research (research design, sample size, location, study period, and risk of bias), and characteristics of participants.

Quality control

To assess the quality of the methodology and bias risk, each observation study was evaluated using a tool developed by Hoy et al; this 10-item scale evaluated the quality of the study in two dimensions, including external credentials (items 1 to 4 target populations, sampling frame, sampling method, and minimum indirect neglect) and internal validity (items 5 up to 9 covering methods for data collection, case definition, study tools, and data collection mode and item 10 covering assessing relevant assumptions or

analyzes). The risk of abuse was assessed by two researchers separately and possible disparity of ideas was resolved by consensus.

Aggregation of data

All eligible studies were included within the systematic review. The data was combined using forest plot graph; random effects model was used to evaluate Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients. The heterogeneity of primary studies was assessed by performing I^2 tests. Meta-analysis was performed using the STAT 14 statistical software.

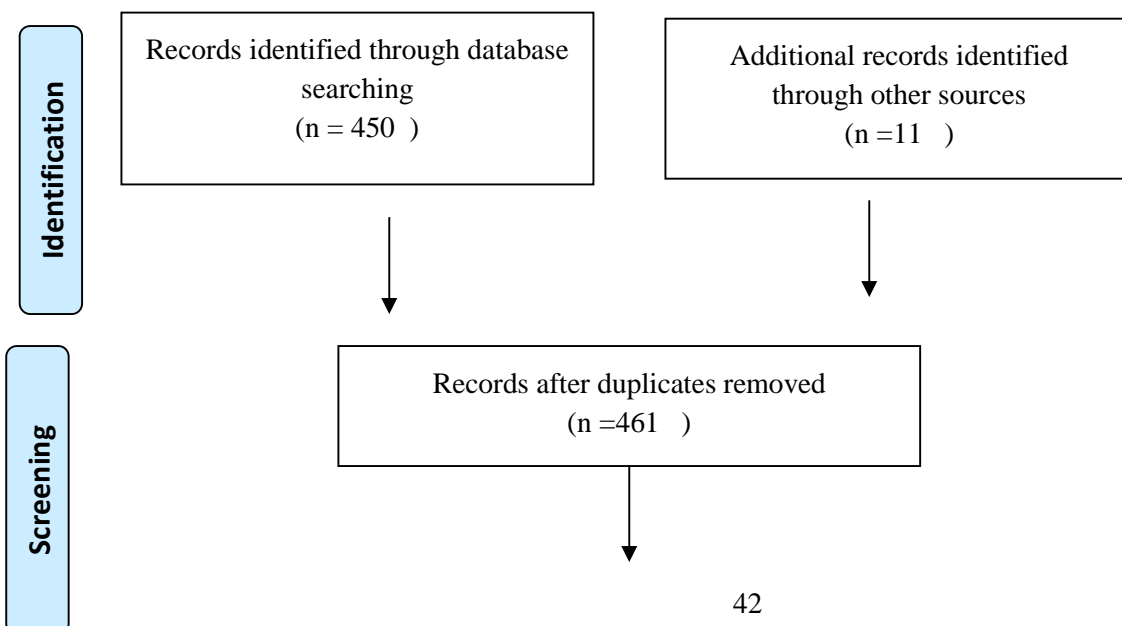
Results

1. Selecting eligible papers and researches

In the initial search on various databases, a total of 461 articles were reviewed, 432 of which turned out to be repetitive during screening process of title and abstract. 19 articles were removed due to unrelated title; out of the remaining 10 articles, 5 articles met the inclusion criteria. Of the 5 articles that were removed, 1 were reviews, 1 were letters to editors, 2 had no complete text, and 1 had low quality and could not be considered in the research. (Figure 1).



PRISMA 2009 Flow Diagram



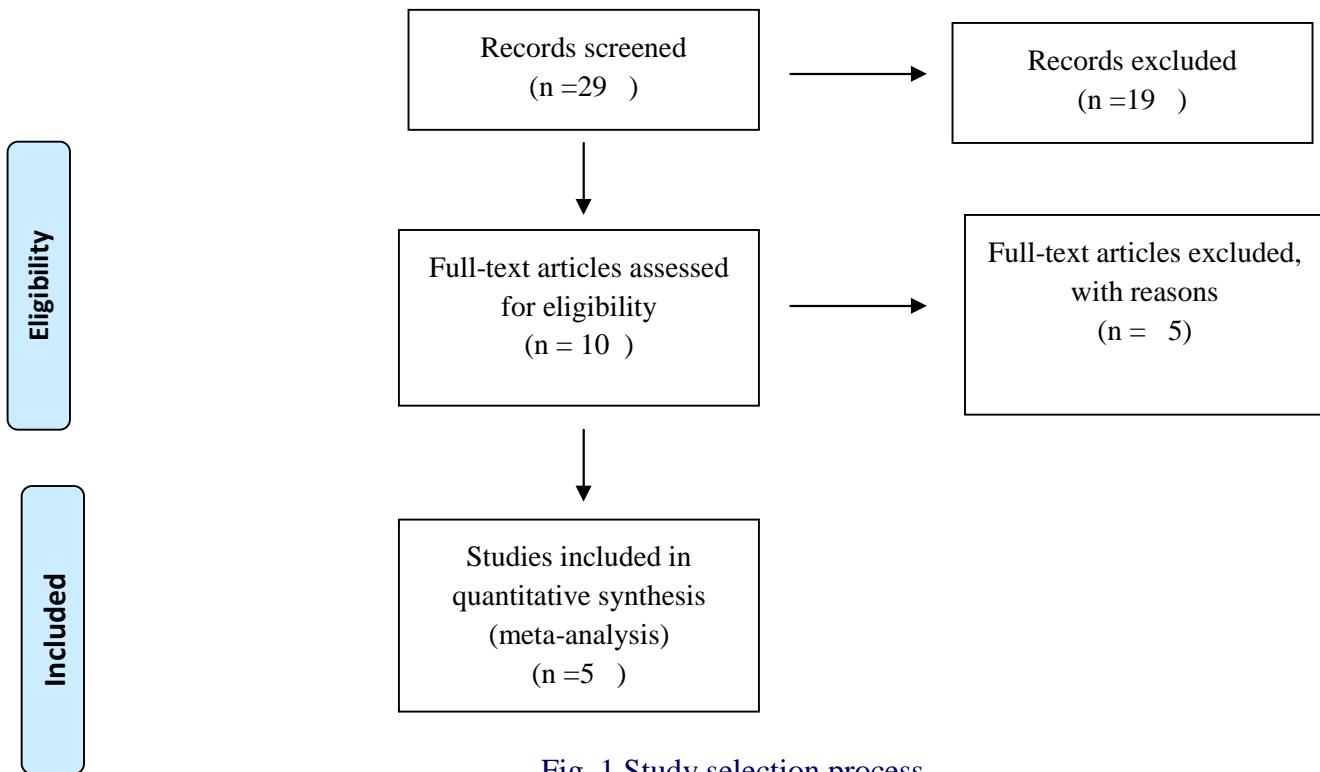


Fig. 1 Study selection process

2. Characteristics of the researches and papers

The final research was conducted on 2273 participants; with an age range of 10 to 60 years old; a cross-sectional design was used in all

studies. Research was conducted in only 2 provinces out of 31 provinces of Iran. Of the 5 studies, four were from Tehran, one from Isfahan. Required data was collected through interview (n = 5) and had a low bias risk (n = 3) (Table 1).

Table 1: Characteristics of final included studies about Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients

| ID | Author | Year | N | Female to male | Province | Prevalence | Bias |
|----|-------------|------|------|----------------|----------|------------|----------|
| 1 | Esfandiyari | 2007 | 179 | 3.26 | Tehran | 10.6 % | Low |
| 2 | Lasemi | 2011 | 400 | 2.7 | Tehran | 13.3 % | Low |
| 3 | Soltanzade | 2008 | 1069 | 3.34 | Tehran | 5 % | Moderate |
| 4 | Koushki | 2014 | 500 | 3.16 | Isfahan | 4 % | Moderate |
| 5 | Darbandi | 2005 | 125 | 1.35 | Tehran | 11.2 % | Low |

Meta-analysis Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients:

Based on the results of random effects model, the Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients in 2273 patients was 5.8% (95% confidence interval [CI]: 4.9, 6.7, $I^2 = 88%$) (table 2).

Table 2: Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients

| Study | Year | ES | 95% conf. Interval | | % weight |
|-----------------------------|-------|-------|--------------------|-------|----------|
| | | | Low | Up | |
| Esfandiyari ^[26] | 2007 | 0.106 | 0.061 | 0.151 | 4.41 |
| Lasemi ^[27] | 2011 | 0.133 | 0.100 | 0.166 | 8.18 |
| Soltanzade ^[28] | 2008 | 0.050 | 0.037 | 0.063 | 53.62 |
| Koushki ^[29] | 2014 | 0.040 | 0.023 | 0.057 | 30.86 |
| Darbandi ^[30] | 2005 | 0.112 | 0.057 | 0.167 | 2.94 |
| Pooled RR | ----- | 0.058 | 0.049 | 0.067 | 100 |

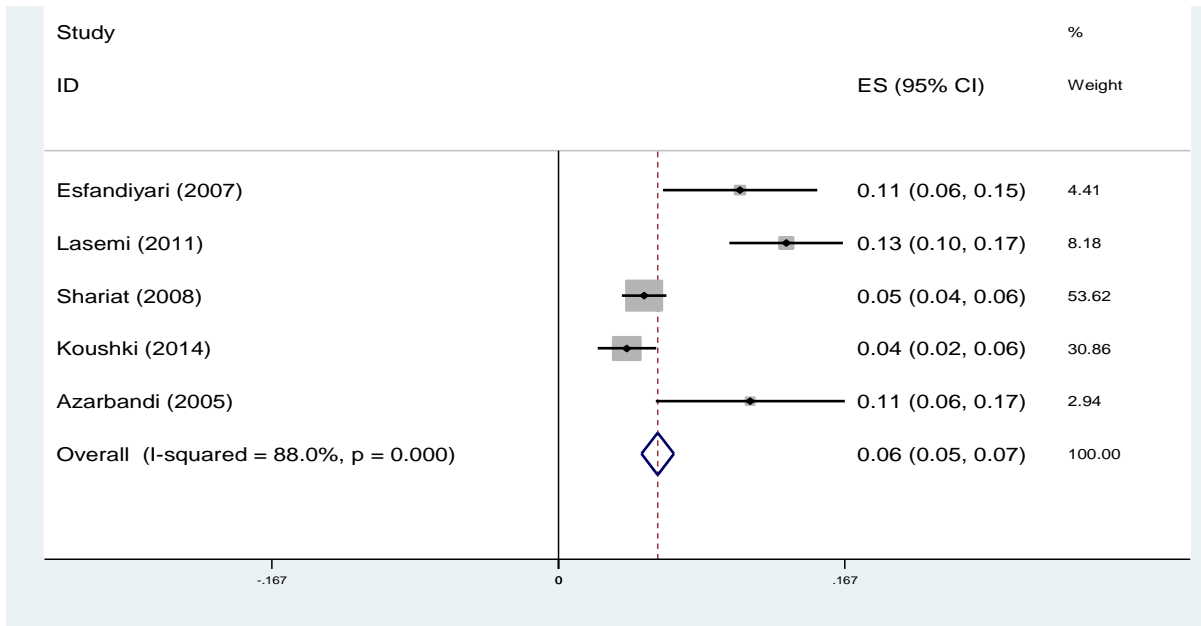


Fig. 2 : The Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients and its 95% interval for the studied cases according to the year and the city where the study was conducted based on the model of the random effects model. The midpoint of each section of the line estimates the % value and the length of the lines showing the 95% confidence interval in each study.

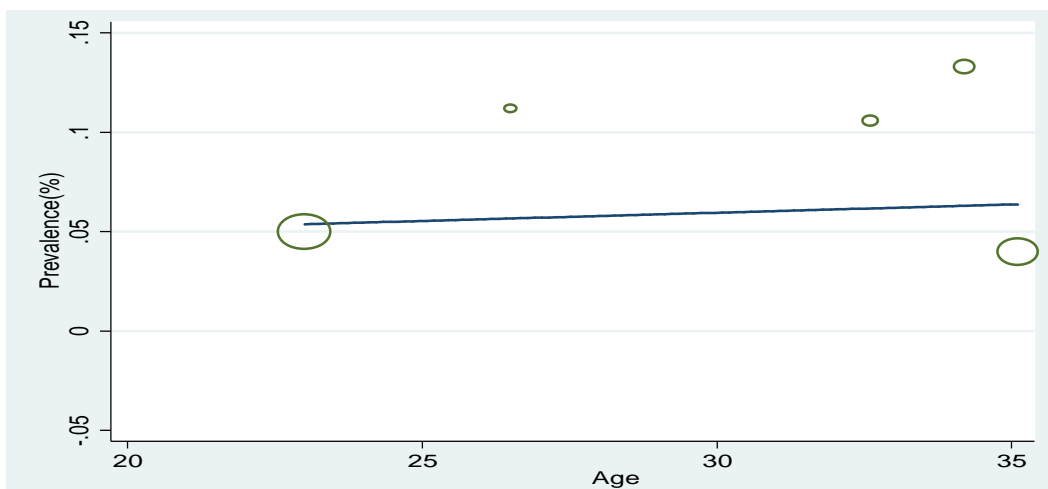


FIG. 3. Meta-regression between age (years) and Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients

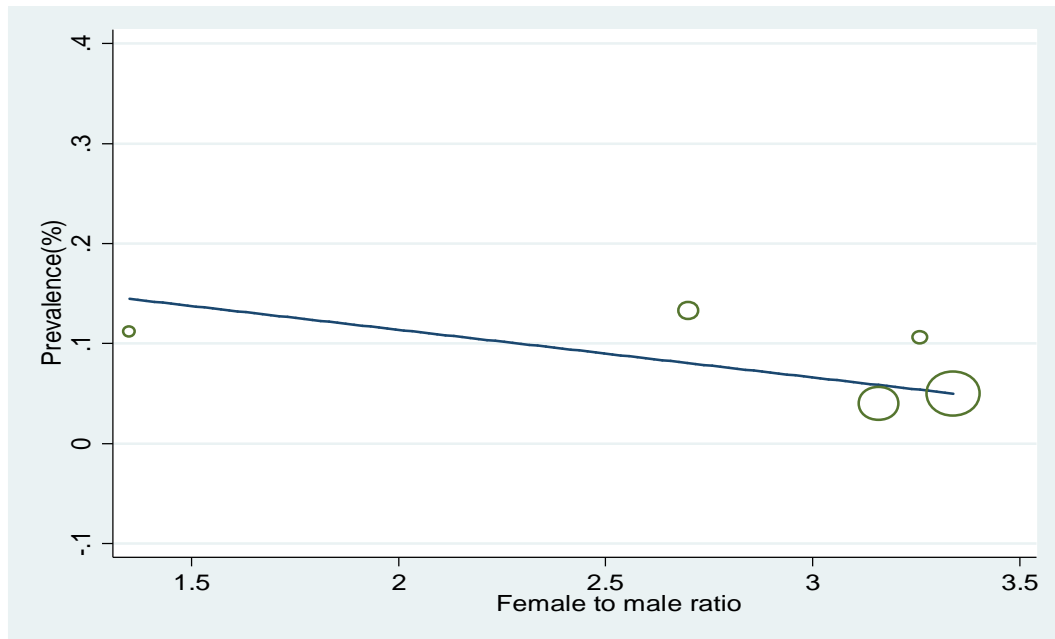


FIG. 4. Meta-regression between the female-to-male ratio and the Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients

Discussion

According to the results of various formerly conducted studies, MS is more common in women than men; despite the lack of any definitive reason for this difference, the interactions between hormonal and immune systems can be effective in this regard(20-22). MS has a recovery and reversal period and it causes irreversible neurological damage during time(23). There would be better prognosis in case of the early diagnosis, especially in women under 40 years of age with limited progression of the disease(24 and 25). The difference in the prevalence of trigeminal neuralgia in MS patients may be due to the difference in the population of the patients (in terms of number, race, geographical area, etc.).

Based on the results of random effects model, the Prevalence of trigeminal neuralgia in Iranian multiple sclerosis patients in 2273 patients was %05.8 (95% confidence interval [CI]: 4.9, 6.7, $I^2 = 88\%$).

Limitations

The most important limitations of the present study were:

A. although We searched different databases, the

information resources in this title were limited.

B. all of the included studies were performed in one country

C. contacting some of the authors because of the lack of information in their studies.

Strengths

A. The present study is the first systematic review study for this purpose.

B. Use of systematic review approach for searching and organizing studies

Conclusion

The prevalence of trigeminal neuralgia in patients with multiple sclerosis turned out to be 5.8% in the present study. This issue highlights the need for physicians to be aware of the causes of facial atypical pain, including triple-nerve pain, especially in patients under 40 years of age. Adequate knowledge and timely diagnosis of trigeminal neuralgia, as the first symptom of MS disease, can help physicians diagnose the disease timely; in case of positive diagnosis, the physicians can start treatments rapidly, avoiding the use of inappropriate and unnecessary therapies.

References

1. Sandell T, Eide PK. The effect of microvascular decompression in patients with multiple sclerosis and trigeminal neuralgia. *Neurosurgery*. 2010 Sep 1;67(3):749-54.
2. Montano N, Papacci F, Cioni B, Di Bonaventura R, Meglio M. What is the best treatment of drug-resistant trigeminal neuralgia in patients affected by multiple sclerosis? A literature analysis of surgical procedures. *Clinical neurology and neurosurgery*. 2013 May 1;115(5):567-72.
3. Tuleasca C, Carron R, Resseguier N, Donnet A, Roussel P, Gaudart J, Levivier M, Régis J. Multiple sclerosis-related trigeminal neuralgia: a prospective series of 43 patients treated with gamma knife surgery with more than one year of follow-up. *Stereotactic and functional neurosurgery*. 2014;92(4):203-10.
4. Jamebozorgi K, Haghghi AB, Yousefipour GA, Kamkarpour A. Atypical basal ganglia germ cell tumor presenting as cerebral and brainstem hemiatrophy. *The neurologist*. 2011 Mar 1;17(2):107-8.
5. Mills RJ, Young CA, Smith ET. Central trigeminal involvement in multiple sclerosis using high-resolution MRI at 3 T. *The British journal of radiology*. 2010 Jun;83(990):493-8.
6. Cruccu G, Finnerup NB, Jensen TS, Scholz J, Sindou M, Svensson P, Treede RD, Zakrzewska JM, Nurmikko T. Trigeminal neuralgia: New classification and diagnostic grading for practice and research. *Neurology*. 2016 Jul 12;87(2):220-8.
7. Truini A, Prosperini L, Calistri V, Fiorelli M, Pozzilli C, Millefiorini E, Frontoni M, Cortese A, Caramia F, Cruccu G. A dual concurrent mechanism explains trigeminal neuralgia in patients with multiple sclerosis. *Neurology*. 2016 May 4;10:212.
8. Jamebozorgi K, Taghizadeh E, Rostami D, Pormasoumi H, Barreto GE, Hayat SM, Sahebkar A. Cellular and Molecular Aspects of Parkinson Treatment: Future Therapeutic Perspectives. *Molecular neurobiology*. 2018 Nov 5:1-3..
9. Javan MR, Nezhad AJ, Safa A, Mohammadi MH, Jamebozorgi K. Personalized Medicine Toward Multiple Sclerosis; Current Challenges and Future Prospects. *International Journal of Basic Science in Medicine*. 2017 Jan 1;2(1):11-5..
10. Zakrzewska JM, McMillan R. Trigeminal neuralgia: the diagnosis and management of this excruciating and poorly understood facial pain. *Postgraduate medical journal*. 2011 Jun 1;87(1028):410-6.
11. Chen DQ, DeSouza DD, Hayes DJ, Davis KD, O'Connor P, Hodaie M. Diffusivity signatures characterize trigeminal neuralgia associated with multiple sclerosis. *Multiple Sclerosis Journal*. 2016 Jan;22(1):51-63.
12. Verheul JB, Hanssens PE, Te Lie S, Leenstra S, Piersma H, Beute GN. Gamma Knife surgery for trigeminal neuralgia: a review of 450 consecutive cases. *Journal of neurosurgery*. 2010 Dec 1;113(Special_Supplement):160-7.
13. Weller, M., Marshall, K., Lovato, J.F., Bourland, J.D., Munley, M.T., Shaw, E.G., Tatter, S.B. and Chan, M.D., 2014. Single-institution retrospective series of gamma knife radiosurgery in the treatment of multiple sclerosis-related trigeminal neuralgia: factors that predict efficacy. *Stereotactic and functional neurosurgery*, 92(1), pp.53-58.
14. Lummel N, Mehrkens JH, Linn J, Buchholz G, Stahl R, Bochmann K, Brückmann H, Lutz J. Diffusion tensor imaging of the trigeminal nerve in patients with trigeminal neuralgia due to multiple sclerosis. *Neuroradiology*. 2015 Mar 1;57(3):259-67.
15. Abhinav K, Love S, Kalantzis G, Coakham HB, Patel NK. Clinicopathological review of patients with and without multiple sclerosis treated by partial sensory rhizotomy for medically refractory trigeminal neuralgia: a 12-year retrospective study. *Clinical neurology and neurosurgery*. 2012 May 1;114(4):361-5.
16. de Sa JC, Airas L, Bartholome E, Grigoriadis N, Mattle H, Oreja-Guevara C, O'Riordan J, Sellebjerg F, Stankoff B, Vass K, Walczak A. Symptomatic therapy in multiple sclerosis: a review for a multimodal approach in clinical practice. *Therapeutic advances in neurological disorders*. 2011 May;4(3):139-68.
17. Kister I, Caminero AB, Monteith TS, Soliman A, Bacon TE, Bacon JH, Kalina JT, Inglese

- M, Herbert J, Lipton RB. Migraine is comorbid with multiple sclerosis and associated with a more symptomatic MS course. The journal of headache and pain. 2010 Oct 1;11(5):417-25.
18. Zakrzewska JM, Akram H. Neurosurgical interventions for the treatment of classical trigeminal neuralgia. Cochrane Database of Systematic Reviews. 2011(9).
 19. Birnbaum G, Iverson J. Dalfampridine may activate latent trigeminal neuralgia in patients with multiple sclerosis. Neurology. 2014 Oct 28;83(18):1610-2.
 20. Harries AM, Mitchell RD. Percutaneous glycerol rhizotomy for trigeminal neuralgia: safety and efficacy of repeat procedures. British journal of neurosurgery. 2011 Apr 1;25(2):268-72.
 21. Jawahar R, Oh U, Yang S, Lapane KL. A systematic review of pharmacological pain management in multiple sclerosis. Drugs. 2013 Oct 1;73(15):1711-22.
 22. Smith ZA, Gorgulho AA, Bezrukiy N, McArthur D, Agazaryan N, Selch MT, De Salles AA. Dedicated linear accelerator radiosurgery for trigeminal neuralgia: a single-center experience in 179 patients with varied dose prescriptions and treatment plans. International Journal of Radiation Oncology* Biology* Physics. 2011 Sep 1;81(1):225-31.
 23. Truini A, Galeotti F, Cruccu G. Treating pain in multiple sclerosis. Expert opinion on pharmacotherapy. 2011 Oct 1;12(15):2355-68.
 24. Lutz J, Linn J, Mehrkens JH, Thon N, Stahl R, Seelos K, Brückmann H, Holtmannspötter M. Trigeminal neuralgia due to neurovascular compression: high-spatial-resolution diffusion-tensor imaging reveals microstructural neural changes. Radiology. 2011 Feb;258(2):524-30.
 25. Seixas D, Foley P, Palace J, Lima D, Ramos I, Tracey I. Pain in multiple sclerosis: a systematic review of neuroimaging studies. NeuroImage: Clinical. 2014 Jan 1;5:322-31.
 26. Esfandiari F, Rezaie M, Amin Tavakoli M, Valizadeh T, Amin Tavakoli N. Frequency of Trigeminal Neuralgia in Patients with Multiple Sclerosis referred to MS Society of Iran in 2004-2005. (in persian)
 27. Lasemi E, Sahraian M, Kalantarmotamedi S, Velaie N, Moradi N, Lasemi R. Evaluation of the frequency of oral-facial manifestations in patients with multiple sclerosis. (in persian)
 28. Soltanzadeh A, Sharifi M, Ilkhchoui Y, Sikaroodi H. Isolated facial palsy in Iranian multiple sclerosis patients. Neurol Asia. 2008 Jun 1;13:73-5.
 29. Koushki MM. Association between trigeminal neuralgia and multiple sclerosis: A population-based study. Multiple sclerosis and related disorders. 2014 Nov 1;3(6):740.
 30. Darbandi A, Rezaie Sh. Prevalence of Trigeminal Neuralgia in Multiple Sclerosis Patients Referring to MS Society of Iran in 2005. (in persian)

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