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PHARMACOLOGICAL TREATMENTS AVAILABLE IN BRAZIL FOR MULTIPLE SCLEROSIS PATIENTS: INTEGRATIVE REVIEW

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ABSTRACT

Introduction: Multiple sclerosis (MS) affects a large number of people worldwide, in Brazil the estimate is 40,000 people who have the disease. There is no cure for multiple sclerosis, but currently there are several treatments available both by the public network and by the private network in Brazil. *Objective:* It is to know the pharmacological treatments available in Brazil for patients with multiple sclerosis. *Methodology:* Fhi an integrative review of the literature, in the Databases PubMed, capes and VHL. *Result and discussion:* Treatment for multiple sclerosis is divided into imunomodulators that are considered the first-line drugs and exist the second-line. *Conclusion:* Thes medications are effective in controlling multiple sclerosis.

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory, chronic, demyexifying disease of thesistemanervoso central (CNS), causing lesions in the brain, spinal cord and optic nerve. The diagnosis is made by the McDonald criteria conjunction with laboratory tests, cerebrospinal fluid, brain and spinal cord images through magnetic resonance imaging and anamnesis of the patient(SILVA e SILVA, 2014). That is, multiple sclerosis is one of the most common causes of chronic neurological disability in young adults (MOREIRA *et al*., 2000). Therefore, according to Yoo (2019) the classification of MS is based according to clinical evolution. In fourforms s that are: remitente-recurrent (EMRR), primarily progressive (EMPP), primarily phased with outbreak (EMPS) and secondarily progressive (EMSP). Being the most common is EMRR, refletindo 85% of cases at the beginning of its presentation. In this sense, according to Santos e Vivan (2018) the treatment is performed throughimmuno modulators, anti-inflammatory drugs, immunosuppressants and several other drugs that help, in reducing symptoms related to the evolution of the disease. Thus, in the scope of public health in Brazil, Law 8,080 was established in 1990, which constituted the Unified Health System (SUS) that have principles on Universality, Integrality and Equity(BRASIL, 2020).

But also, characterizing what the 196art. of the 1988 Constitution recommends, health is a right of all and the duty of the State(BRASIL,1998). That is, the specific obtaining of medicines is guaranteed through two public health policies, the National Drug Policy(BRASIL, 1998), as well as theN-acionalPolicyof The Farmacêutitica(CNS, 2004). However, according to Soárez*et al*.,(2014) recently, the SUS has been showing some challenges with regard to its sustainability, includingensuring it's financing. Therefore, drug treatment has as its main objective s, to improve the patient'sclinic, as well as increased functional capacity, reduction of comorbidity and reduction of symptoms. The main drugs used in this case are: Beta-interferons, glatirâmercetate, eriflunomide t, dimethyl fumarato, fingolimode, natalizumab, lentuzumab (CONITEC, 2022). However, according to Volpi *et al*., (2019) intestinal dysfunction in patients with MS is most often involved, with the administration of multiple medications, as well as infection, severe liverinjury, severe anemia and hemolytic anemia, are some of the adverse effects of treatmentof patients with multiple sclerosis. So, the therapeutic approach of MS has been immunosuppression, with the objective of reducing inflammatory damage caused by immune cells within the CNS,adaptive immunological responses occur, immunosuppressive agents impair the activation and proliferation of T and B lymphocytes(VOLPI *et al*, 2019).

Figure 1. Obtaining scientific articles

N	Title	Authors	Year	Periodic	Goal	Result
1	Oral cladribine for the treatment of relapsing-recurrent multiple sclerosis highly active: impact analysis from the perspective of the system Braziliansupplementaryhealth	Leticia Jabase, Gabriel Leonel Marasco, Ana Carolina Padula Ribeiro-Pereira, Leonardo Valente Camargo, Giovanna ReneloPuopolo, Roberta Arinelli Fernandes, Alexander Chehin	2021	JBES	Assess the budgetary impact of the inclusion of oral cladribine in the treatment of sclerosis reactive-recurrent multiple multiple in high disease activity (EMRR HDA) in the Supplementary Health System (SSS).	The incremental cost of cladribine inclusion for the SSS was estimated at 463,265 BRL, 739,691 BRL, -1,414,963 BRL, -3,719,007 BRL, in years 1, 2, 3 and 4, respectively. This resulted in a total incremental cost of -3,931,015 BRL in the period represented by 1.5% of the total budget reduction in the treatment of EMRR HDA.
2	Efficacy and Adverse Events of The Use of Natalizumab in a Brazilian Cohort of Patients with Multiple Sclerosis	M.Q. Deslandes , P.T. Alves, M.P. Alvarenga, V.CC Lessa, S. Camargo, R.MP Alvarenga, Claudia C. Vasconcelos	2020	Elsevier	evaluated the efficacy and adverse events of NTZ in a cohort of Brazilian patients with MS, as well as the impact of clinical and demographic factors on the patient's response to treatment.	The study involved 56 patients; 64% were women and 36% were Afrodescendants. There was a significant reduction in the mean absolute number (P = 0.001) and in the annualized rate (P = 0.001) of recurrences and in the radiological activity of the disease (P = 0.001). In addition, 71% of the patients did not present an increase in the score of the Expanded Disability Status Scale after 1 year of treatment. The efficacy of NTZ was not associated with the presence of prognostic clinical and demographic factors, and the most frequent adverse events during NTZ use were gastrointestinal symptoms; there have been no cases of progressive multifocal leukoencephalopathy .
3	Profile of patients diagnosed with multiple sclerosis in a city in the Southern region ofBrazil	Barbara Biffi Gabardo, Everton Paulo Roman, RenattoEndlerIachinsk, HeboniSabadin, Leonardo Silva Grassi, João Pedro Zanatta, Layane Sanches Fernandes	2020	ResearchSociety and Development	Analyze the profile of patients with MS in the last 7 years in 3 service centers located in the city of Cascavel, western Paraná, Southern Brazil.	The first symptoms were motor/sensory, visual or headache and about 50% were diagnosed with in less than 1 year. The mean age of diagnosis of the patients was 34.8 years. It was found that 67.9% had or have already underwent psychological treatment. Treatment ms, the use of glatirâmer acetate, β interferon 1a and natalizumab predominated among patients.
4	Evaluation of diagnostic practices and treatment of Brazilian neurologists among patients with multiple sclerosis	Cássia Elisa MARIN, Dagoberto CALLEGARO, Marco Aurélio LANA-PEIXOTO, Oscar FERNÁNDEZ, Antônio Pereira GOMES NETO, Claudia Cristina Ferreira VASCONCELOS, José Artur Costa D'ALMEIDA, Marco Vinícius Magno GONÇALVES, Maria Fernanda MENDES, Mônica Koncke Fiuza PAROLIN, OsvaldoNascimento, Paulo Diniz DA GAMA, Rafael Paternò Castello DIAS-CARNEIRO, Ronaldo Maciel DIAS, Alfredo DAMASCENO, Jefferson BECKER	2020	ScieloBrazil	Investigate factors considered by Brazilian neurologists in the management of MS and identify how contribute to diagnosis and treatment.	Neurologists from 13 Brazilian states answered the survey (n = 94). In the clinically isolated syndrome (ISC) scenario, the interviewees agreed to treat patients at high risk diagnosis of MS, while in radiologically isolated syndrome (RIS) half of the interviewees chose not to treat, even among patients high-risk. In cases of low-activity reactive-reactive MS (RRMS), treatment choice was distributed among interferon beta, acetate glatiramer and teriflunomide, which were changed to fingolimode and natalizumab as the severity of RRMS increased. The topics in that there was disagreement included practices on the use of disease-modifying therapy (TDD) for pregnant patients and washout.

| 5 | Brazilian Consensus for the Treatment of Multiple Sclerosis: Brazilian Academy of Neurology and Brazilian Committee for Treatment and Research in Multiple Sclerosis | Vanessa Daccach Marques, Giordani Rodrigues dos Passos, Maria Fernanda Mendes, Dagoberto Callegaro, Marcus Aurelius Lana-Peixoto, Elizabeth Regina Comini-Fleet, Cláudia Cristina Ferreira Vasconcelos, Douglas Kazutoshi Sato, Maria Lúcia Brito Ferreira, Monica Koncke Fiuza Parolin, Alfredo Damasceno, Anderson KuntzGrzesiuk, André Muniz, André Palma da Cunha Matta, Bianca Etelvina Santos de Oliveira, Carlos Bernardo Tauil, Damacio Ramón Kaimen Maciel, Denise Sisteroli Diniz, Eber Castro Corrêa, Fernando Coronetti, Frederico M. H. Jorge, Henry Koiti Sato, Marcus Vinícius Magno Gonçalves, Nise Alessandra de C. Sousa, Osvaldo J. M. Nascimento, Paulo Diniz da Gama, Renan Domingues, Renata Faria Simm, Rodrigo Barbosa Thomaz, Rogério de Rizo Morales, Ronaldo Maciel Dias, Samira dos Apóstolos-Pereira, Suzana Costa Nunes Machado, Thiago de Faria Junqueira, Jefferson Becker | 2020 | ScieloBrazil | Prescribe MS DMTs according to what is best for each patient, and evidence-based and up-to-date practices. | Through this document, we propose practical recommendations for the treatment of MS, with a main focus on the choice and management of MDTs, and review the arguments that support the treatment strategies in MS. |
| 6 | The Assessment for Intramuscular Interferon Disinvestment Beta for Remiscurrent Multiple Sclerosis in Brazil | Livia Lovato Pires de Lemos, Augusto Afonso Guerra Junior, Marisa Santos, Carlos Magliano, Isabela Diniz, Kathiaja Souza, Ramon Gonçalves Pereira, Juliana Alvares, Brian Godman, Marion Bennie, Ivan Ricardo Zimmermann, Vânia Cristina Canuto dos Santos, Clarice Alegre Pretramale, Francisco de Assis Acurcio | 2018 | Springer link | Describe the disinvestment process of IFN-β-1a-IM in Brazil. The first evaluation was composed of a literature literature review and meta-analysis of mixed treatment comparison. | CONITEC commissioned a study to evaluate the efficacy of IFN-β-1a-IM among Brazilian patients in routine clinical care. The second evaluation involved an 11-year follow-up of a non-simultaneous cohort of 12,154 MS patients developed by deterministic-probabilistic linkage of the administrative databases of the SUS. The real-world evaluation also showed that users of IFN-β-1a-IM presented a statistically higher risk of treatment failure, defined as switching treatment or treatment of relapse or death, with the evaluation showing that IFN-β-1a-IM was lower than other IFN-βs and glatiramer acetate in direct and indirect analysis. In the drug ranking with 40,000 simulations, ifn-β-1a-IM was the worst option, with a success rate of only 152/40,000. Conitec then decided to exclude the intramuscular presentation of IFN-β from current Guidelines for Treatment of MSM, giving patients who are currently in this treatment the option of continuing until treatment failure. |

Source: The authors themselves, 2022

In view of this, this article seeks to deepen the importance in relation to the study of drugs used by patients with multiple sclerosis, which are the main adverse events of them and which of these drugs to understand (PCDTEM). Therefore, the aim of this study was to conduct an integrative review of the literature, in order to know the pharmacological treatments available in Brazil for patients with multiple sclerosis (MS).

METHODOLOGY

This is an integrative review of the literature on pharmacological treatment s to patients with neurological disease of multiple sclerosis (MS), especially in Brazil. That is, integrative review is considered an enriching process to science, by "combining data from theoretical and empirical literature and incorporating a range of purposes: definition of concepts; review of theories and evidence; and analyze problems [...] (SOUZA, SILVA e CARVALHO 2010). In this sense, according to Silva (2015) descriptive research interprets, moreover, four points of view on this theme: description, record, analysis and interpretation of current events, thus aiming at conducting the present. For example, step for the elaboration of an integrative review is a research method that allows: 1- Fromweaving the theme and choosing the research-based question; 2- Amostra orbusca in the literature; 3- Classification when to studies; 4- Thenalise of the studies included; 5- Studies of results; 6) Synthesis ofthe main ideas (MENDES, SILVEIRA e GALVÃO 2008). A survey of the literature was carried out between June and July 2022, and the collection was performed throughthe database: National Library of Medicine National Institutes of Health of the USA (MEDLINE/PUBMED), Regional Portal of the VHL (Virtual Health Library) and the Capes Journals. Therefore, the busca by the articles was performed through the D writers of Science of Saúde (DeCS) of the virtual library in vHLhealth, in the Portuguese languageand English: multiple sclerosis 'multiple sclerosis', treatment 'treatment', diagnosis 'diagnosis' , Brazil 'Brazil' and utilizado the Boolean operator 'AND'. The calculation of these articles involved the exclusion of repetitive, incomplete studies, which were not aligned according to the main objective of the research, congress proceedings, review articles. The inclusion was the articles in the Portuguese, English and Spanish, of the last five yearsthat addressed the theme of the research, as well as originals, randomizedstudy, cohort study, books. Therefore, in the search conducted in the database, 179 articles were found, atthe end 6 articles were selected and included according to the eligibility criteria to make up the sample of this integrative literature review.

RESULTS

In the presentation of the results obtained that composes this article, the main elements of the six texts included in this qualitative synthesis are presented, namely: Describing the distribution of publications by title, author(s), year, journal; proposed objectives and results obtained. For the best organization of such information, the results of the present study were organized in table 1, presented below.

DISCUSSION

The aim of this study was toknow the types of pharmacological treatment available to patients with multiple sclerosis (MS) in Brazil. In this sense, the article by Marin *et al.,* (2021) highlights that in general most Brazilian patientsreceive their medication from the state. This is due to the fact, according to conitec (2022) ofBrazil to provide annacional polytic of the holding to the portador of doença neurological through the unified health system (SUS), among which patients who present with multiple sclerosis. Also, on the treatment of MS in Brazil, Lemos *et al.,* (2018) highlight that the SUS provide three pharmaceutical presentations of interferon beta (IFN-b), as a first-line drug.

As stated, Deslandes *et al.,* (2020) in his article, natalizumab (NZT) was approved by the Ministry of Saúde in Brazil, according to ordinance No. 49, on November 11, 2020. In parallel in his studies Gabardo *et al.,* (2020) found that most patients with MS use the following drugs in their pharmacological treatment: glatirâmer acetate, β-interferon, natalizumab, fumarate dimethyl, ocrelizumab, teriflunomide, azathioprina, fingolimode, the latter being the least used by the Brazilian population. Glatirâmer, beta interferon and teriflunomide are considered the first-line drugs. In cases of drug failure, drug intolerance, adverse reactions or non-adherence, there is a replacement of the first-line drug, which may be by the drugs Fingolimode or natalizumab (Clinical Protocol and Multiple Sclerosis Therapeutic Guidelines, 2018). However, according to Marin *et al.,* (2021) treatment during pregnancy can be seen in some specific cases, as examples natalizumab and alemtuzumab can be seen after a debate about the potential implications of thesedrugs, fetal development. In this sense, according to Jabase *et al.,* (2021) it is part of the treatment ofMS in Brazil,the publicand private health system, represented at the federal level by the SUS and also by the Supplementary Health System (SSS). That is, according to Jabase *et al.,* (2021) in 2021 close to 48 million individuals were favored by the SSS, which is equivalent to about 25% of the country's population. In this scenario, accordingto Marques *et al.,* (2018) several patients with multiple sclerosis (MS), receive disease-modifying therapy (TDDs) in the public health system. For example, according to Marques *et al.,* (2018) alemtuzumab demonstrated that patients previously treated with this drug in the case of MS, presenta high efficacy in their results. Therefore, according to Marques *et al.,* (2018)treatment with interferon beta, glatiramer acetate, dimethyl fumarate or teriflunomide, which often have a greater safety character and are often more easily accessible (included in the Brazilian public health system).

CONCLUSION

This article highlighted research demonstrating whichdrugs are available in Brazil for patients with MS. Theyseek to decrease the inflammatory action, as well as their symptoms. Thus, multiple sclerosis is a disease that until this time, still has no cure. Atthis time is available an extensive range of treatments, which should be pertinent to the patient according to his need. Therefore, it is pertinent to point out that the choice of treatment is complex: and manycases, the patient should do tests with several drugs until he discovers the most convenient for it, due tothe widenumber of drug options.

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