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EFFICACY OF AUTOLOGOUS BONE MARROW TRANSPLANTATION IN THE TREATMENT OF MULTIPLE SCLEROSIS: AN INTEGRATIVE REVIEW

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Abstract: Introduction: Multiple sclerosis is an autoimmune neurological disease defined as an inflammatory disorder of the brain and spinal cord. One treatment option is the use of mesenchymal stem cells from autologous bone marrow transplantation. **Objective: To** identify the effectiveness of autologous bone marrow transplantation in the treatment of multiple sclerosis. **Method:** This integrative review used the PubMed/MEDLINE and Virtual Health Library (VHL) search engines in April and May 2021 using the descriptors "*bone marrow*" AND "*multiple sclerosis*" AND "*transplantation*" AND (*therapeutics* OR *treatment*), with the NOT *review* descriptor added to PubMed. Articles from 2016 to 2021 with full text available were included, and the human limit was selected. Only the MEDLINE database was used and the main subjects selected were Multiple Sclerosis and Autoimmune Diseases. Inclusion and exclusion criteria were applied, determining the articles that make up this review. **Results:** In general, the articles analyzed showed that autologous bone marrow transplantation is relatively stable and effective. The best results were achieved in the long term and post-transplant patients had high rates of neurological progression-free survival, based on follow-up using the Kurtzke Expanded Disability Status Scale. **Conclusions:** The treatment of multiple sclerosis is still the subject of extensive debate and autologous bone marrow transplantation appears to be an option. In general, positive results have been found for this therapy. However, the studies indicate the need for further clarification of its efficacy and safety.
Keywords: Multiple sclerosis. Bone Marrow. Transplant. Treatment.

INTRODUCTION

Multiple sclerosis (MS) is an autoimmune neurological disease defined as an inflammatory disorder of the brain and spinal cord, with damage to the myelin sheath and axons due to focal lymphocytic infiltration. MS manifests itself mainly through episodic neurological dysfunctions with subsequent remission, known as relapsing-remitting MS. Other possibilities are manifestation in the form of progressive dysfunctions without remission, called primary progressive MS, or in the initial remitting form followed by progressive, called secondary progressive MS. In all forms, the evolution of the disease makes neurodegeneration extensive and chronic (COMPSTON; COLES, 2008; KELSEY *et al.*, 2016). According to the MS Atlas drawn up by the International Multiple Sclerosis Federation (2020), the disease affects 2.8 million individuals globally. It mainly affects young adults of working age, with an average diagnosis age of 32.

Its etiology involves exposure to environmental factors in individuals with susceptible genetic profiles. Its incidence is higher in countries with a cold climate, suggesting a relationship with low sun exposure and vitamin D deficiency. It has also been shown, for example, that infection with the Epstein-Barr virus in young adults increases the risk of developing the disease (COMPSTON; COLES, 2008). The occurrence of symptoms in MS is related to the areas of the central nervous system that have been affected and can vary in severity and duration. The most prevalent symptoms are fatigue, pain, sexual dysfunction, difficulties with movement and motor coordination, urinary problems, intestinal problems, visual problems, cognitive problems and emotional changes (MULTIPLE SCLEROSIS INTERNATIONAL FEDERATION, 2021).

There is currently no cure for MS, but several treatments are recognized, mainly for symptom control, such as the use of medica-

tion to relieve pain and physiological changes, as well as the indication of physiotherapy or occupational therapy to adapt and support the lifestyle of the person with the disease (MULTIPLE SCLEROSIS INTERNATIONAL FEDERATION, 2021), in addition to immunomodulatory and immunosuppressive therapies (KELSEY *et al.*, 2016). The use of mesenchymal stem cells from autologous bone marrow (BM) transplantation is also a treatment option. Even so, the discussion about the efficacy, safety and convenience of each therapy is a source of much debate and study (COMPSTON; COLES, 2008).

In autologous BM transplantation, which is the focus of this study, the donated hematopoietic cells come from the recipient themselves, thus avoiding the risk of transplant rejection caused by histocompatibility antigens. Before bone marrow extraction takes place, apheresis is carried out. In this process, the patient is administered drugs that stimulate the proliferation of stem cells in the blood, which can be repeated several times until the ideal number of stem cells in the bloodstream is reached (REGISTRO NACIONAL DE DOADORES DE MEDULA ÓSSEA, [?]).

The autologous bone marrow extraction procedure is similar to blood transfusion, since both procedures are quick and the extracted content is stored in bags. The stem cells contained in these bags are frozen in liquid nitrogen until they can be used in the donor (RODRIGUES, 2017). In the phase following bone marrow extraction, the patient receives high doses of chemotherapy and/or radiotherapy in order to destroy the immune cells and prepare the body to receive the new cells. Despite being considered a less invasive procedure, the patient is usually affected by the effects of chemotherapy and may experience nausea, loss of appetite, mucositis, diarrhea, constipation and alopecia (ASSOCIAÇÃO DA MEDULA ÓSSEA, [?]).

Autologous BM transplantation is an alternative for MS patients who do not respond to conventional treatment, since according to studies the risk of transmission of infectious diseases is low and the degree of post-transplant complications is lower (GIACOPPO; BRAMANTI; MAZZON, 2017). In this sense, the aim of this review is to identify the effectiveness of autologous bone marrow transplantation in the treatment of multiple sclerosis.

METHODS

This study is an integrative literature review. The PubMed/MEDLINE and Virtual Health Library (VHL) search tools were used for data collection from April 27 to May 25, 2021. The descriptors used indexed in the *Medical Subject Heading* (MeSH) and synonyms in the VHL and PubMed were "*bone marrow*" AND "*multiple sclerosis*" AND "*transplantation*" AND (*therapeutics* OR *treatment*), and in the PubMed search database, in addition to these descriptors, the descriptor NOT *review* was added.

The two databases included articles from 2016 to 2021, in Portuguese, English and Spanish, with full text available, and the human limit was selected. Only MEDLINE was used in the VHL and the main subjects selected were Multiple Sclerosis and Autoimmune Diseases.

After the titles and abstracts were read by pairs of reviewers, review articles, articles that did not address the main topic, studies with animal tests and incomplete texts were excluded. After applying these criteria and excluding duplicates, the selected papers were read in their entirety, and those with insufficient content were excluded, determining which were included in this review.

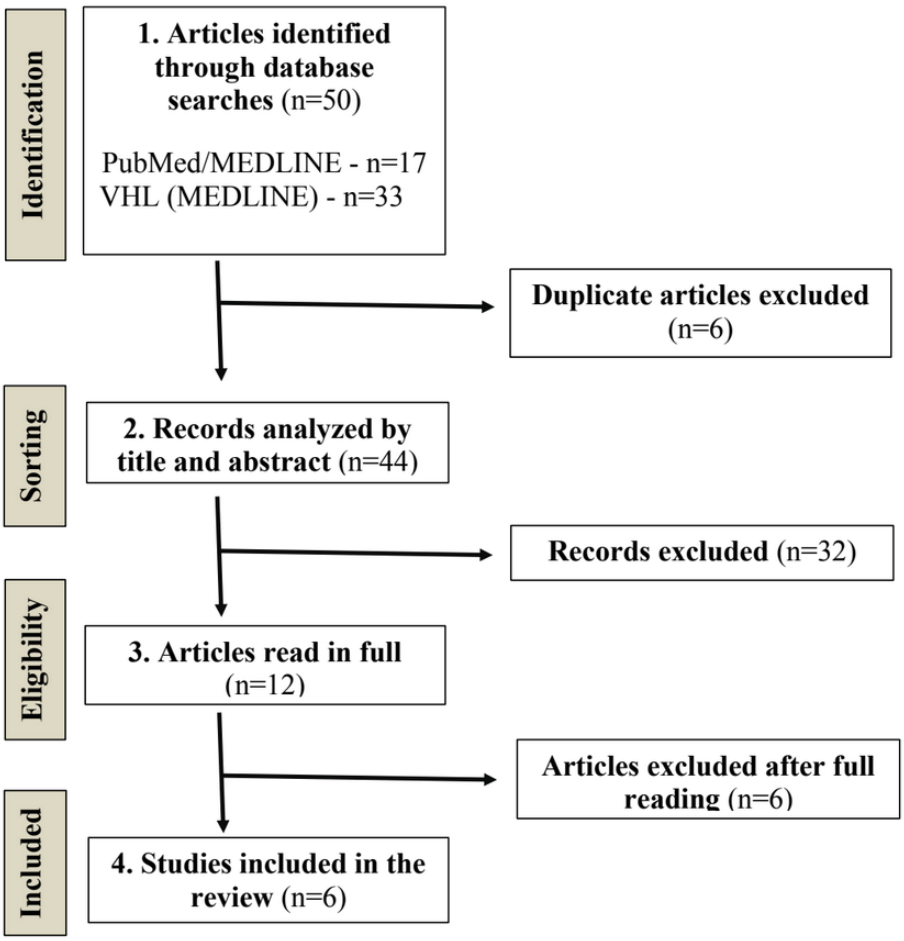

Figure: Flowchart

Source: Prepared by the authors.

Study No.	Authors / Year of publication	Title	Descriptors	Country of study
01	SAHRAIAN *et al.* / 2018	Therapeutic Use of Intrathecal Mesenchymal Stem Cells in patients with Multiple Sclerosis: A Pilot Study with Booster Injection	1. Booster injection 2. Intrathecal mesenchymal stem cells 3. Multiple sclerosis	Iran
02	GUILLAUME--JUGNOT *et al.* / 2019	Autologous hematopoietic stem cell transplantation (AHSCT) in autoimmune disease adult patients in France: analysis of the long-term outcome from the French Society for Bone Marrow Transplantation and Cellular Therapy (SFGM-TC)	1. Adult patients 2. Autoimmune disease 3. Autologous 4. Hematopoietic stem cell transplantation	France
03	MURARO *et al.* / 2017	Long-term outcomes after Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis	None	England
04	COHEN *et al.* / 2018	Pilot trial of intravenous autologous culture-expanded mesenchymal stem cell transplantation in multiple sclerosis	1. multiple sclerosis 2. Clinical trial 3. Mesenchymal stem cells 4. Disability measures 5. Quantitative MRI	United States of America

05	DAHBOUR *et al.* / 2017	Mesenchymal stem cells and conditioned media in the treatment of multiple sclerosis patients: Clinical, ophthalmological and radiological assessments of safety and efficacy	1. Conditioned media 2. Expanded disability status scale 3. Magnetic resonance imaging 4. Mesenchymal stem cells 5. Multiple sclerosis 6. Optical coherence tomography 7. Visual evoked potential	Jordan
06	LEE *et al.* / 2016	Brain atrophy after bone marrow transplantation for treatment of multiple sclerosis	1. multiple sclerosis 2. Magnetic resonance imaging 3. Atrophy 4. Models 5. Statistics 6. Transplantation conditioning 7. Bone marrow transplantation	Canada

Table 1: Included studies classified according to authors, year of publication, title, descriptors and country of study.

Source: Prepared by the authors.

RESULTS

After searching the databases, 50 articles were found, 17 from PubMed and 33 from the VHL. Of these, six duplicate articles were excluded, leaving 44 articles for analysis by title and abstract, 32 of which were excluded. The remaining 12 articles were then read in full, resulting in the exclusion of six. At the end of the selection process, a total of six articles were included in the review. This process is represented by the flowchart (Figure) below.

The six studies included in this review were published between 2016 and 2019. All were published in foreign journals in English. The basic information about each study is described in the table (Table 1) below.

The study by Sahraian *et al.* (2018) was a pilot study on the use of mesenchymal stem cells from autologous OM transplantation. Four patients with MS were studied. Of these, three had secondary progressive MS and one had relapsing-remitting MS. A first injection of the treatment was carried out and partial efficacy was reported, as the number of stable patients decreased over time. The treatment was then re-administered via a booster injection after one year and its safety and efficacy were assessed. None of the patients presented adverse events following OM aspiration. The intrathecal injection was successfully performed in all patients without any major complications.

Patients 01 and 02, both with secondary progressive MS, received a booster injection after one year. Patients 03 and 04, with secondary progressive MS and relapsing-remitting MS, respectively, received a single intrathecal injection. All the patients with secondary progressive MS showed a halt in the progression of the disease and two of them even had improvements in the dysfunctions that already existed before treatment. Patient 04 had been free of flare-ups for two years and, 12 months after the transplant, had a flare-up of the disease, from which he recovered with the use of steroids (SAHRAIAN *et al.*, 2018).

An assessment was made using the Kurtzke Expanded Disability Status Scale (EDSS), which showed that the scores of patients 01 and 02 decreased by 0.5 and 1 point during 2 years of follow-up, respectively, which is positive. Patient 03's score remained unchanged and patient 04's score increased by 0.5 over two years with fluctuation. The MRI assessment did not show the appearance of new or enlarged plaques, which characterizes the non-progression of MS. The authors concluded that the use of mesenchymal stem cells

from autologous OM transplantation can be considered an effective therapy, especially for patients with secondary progressive MS. The use of booster injections has been shown to be safe and may increase the effects of this therapeutic approach (SAHRAIAN *et al*., 2018).

The study by Guillaume-Jugnot *et al.* (2019) retrospectively analyzed the long-term results of autologous BM transplantation in the treatment of autoimmune diseases reported to the French Society of Bone Marrow Transplantation and Cell Therapy (SFGM-TC). The participants included were all French patients with autoimmune diseases treated with autologous BM transplantation until 2013, totaling 94 patients. Of these, 14 had MS.

Primary data was obtained from the registers of the European Society for Marrow and Blood Transplantation (EBMT). Additional data was obtained by applying a questionnaire designed by the authors, based on existing instruments such as the EDSS scale. The primary outcome analyzed was overall survival. Secondary outcomes were progression-free survival, defined as survival without evidence of relapse or progression, and relapse-free mortality, defined as death after transplant not attributed to relapse or progression of the disease. Follow-up revealed: 1. overall survival of 77.4% at 5 years and 64% at 10 years; 2. progression-free survival of 51% at 5 years and 44.1% at 10 years; 3. relapse-free mortality of 8.7% at day 100, 9.8% at 5 years and 13.6% at 10 years (GUILLAUME-JUGNOT *et al.*, 2019).

Only one patient with MS died as a result of relapse or disease progression. According to the authors, MS patients have the lowest risk of death among patients with autoimmune diseases undergoing autologous BM transplantation. The authors concluded that autologous BM transplantation in the treatment of autoimmune diseases such as MS shows long-term benefits with acceptable toxicity (GUILLAUME-JUGNOT *et al*., 2019).

The study by Muraro *et al.* (2017) is a multicenter observational study that collected in 13 countries the evaluation of 281 patients with a predominance (78%) of progressive forms of MS who underwent autologous BM transplantation during the years 1995-2006. Transplant-related mortality was 2.8% and progression-free survival was 46% at five years post-treatment.

To analyze the neurological disability score, the EDSS scale was used before and after the transplant. We analyzed 111 patients who met the evaluation requirement of an EDSS score three years before transplantation and post-treatment by the proposed dates. In this evaluation, it was observed that 12 months before the transplant there was an increase of 0.94 points in the mean EDSS score and in the next 12 months post-transplant there was a decrease of 0.32 points in this mean score. The EDSS score was different between patients with relapsing-remitting MS (one year pre-transplant increased by 1.42 and post--transplant decreased by 0.76) and with the progressive form of MS (one year pre-transplant increased by 0.73 and one year post--transplant decreased by 0.14) (MURARO *et al*., 2017).

During this study, it was observed that almost half of MS patients survived free of progressive neurological disease five years after autologous BM transplantation. Patients with relapsing-remitting MS who were younger, had fewer treatments prior to transplantation and had lower neurological disability scores were associated with better long-term outcomes (MURARO *et al*., 2017).

The study by Cohen *et al.* (2018) evaluated the feasibility, safety and tolerability of autologous mesenchymal stem cell transplantation. During the comparison study, stem cells were infused into 24 patients, 10 with relapsing-remitting MS and 14 with secondary progressive MS. The patients chosen

had a relapse or worsening of the disease. MRI lesion activity in the previous two years and optic nerve involvement were also criteria used. In addition, an EDSS assessment was carried out and the average score obtained by the participants was 5.2.

Exploratory efficacy measures such as self-report, multiple sclerosis status, brain MRI with gadolinium enhancement, number and volume of T1 and T2 lesions, vision and gray matter fraction were used. The aim of the exploration was to assess the effect of transplantation in cases of MS, however, as it was an open pilot study, without a parallel control and not powered to reliably detect temporal trends, values were used to describe the compatibility of the data with the absence of mesenchymal stem cell activity and not for formal hypothesis testing. The primary exploratory value compared slopes or means at three months post-infusion with the period two to three months before infusion (COHEN *et al.*, 2018).

There was no severe acute encephalitis syndrome related to the study. Two participants with secondary progressive MS died; however, the deaths were apparently unrelated to the transplant. No participants developed clinical manifestations or indicated autoimmune phenomena. Of the total number of participants, 75% had no relapses, 12.5% had a single relapse and 12.5% had two relapses. Of the participants affected by relapses, only one did not have relapsing-remitting MS (COHEN *et al.*, 2018).

The authors support the feasibility, safety and tolerability of administering autologous mesenchymal stem cells derived from OM in cases of MS ( ). However, as it was a small study, with only six months of follow-up, they understand that it is not feasible to rule out the appearance of acute encephalitis syndrome afterwards (COHEN *et al.*, 2018).

The study by Dahbour *et al.* (2017) compared the use of interferon and autologous bone marrow-derived mesenchymal stromal cells (BM-MSCs) and mesenchymal stromal cells (MSC-MSCs) in the patients studied, since these have multiple capacities to regenerate affected areas, including neurological ones. 30-50 mL of OM were aspirated from the iliac crest to be isolated and centrifuged to separate the BM-MCs that would be injected intrathecally into the patients. After an interval of one month, a volume of 18 mL of preserved BM-MCs from each patient were thawed and administered intrathecally similar to mesenchymal stromal cells. After each injection and follow-up, the patients returned to the clinic for full examinations.

The examinations were important for checking for any changes that occurred during the study and included clinical, visual, radiological and inflammatory assessments. The evaluation criteria and results are shown in the table (Chart 2) below:

It was found that no patient had a life-threatening event from the time of injection until the year of follow-up, such as encephalopathy, meningitis, allergic reactions or seizures and both BM-MSC and MSC-CM are considered relatively effective in stabilizing the disease, but studies still need to be carried out to better determine the effectiveness of the treatment in combating MS (DAHBOUR *et al.*, 2017).

The study by Lee *et al.* (2017) evaluated the whole brain volume of 19 patients with relapsing-remitting MS and highly active secondary progressive MS with poor prognosis who had progressive disability and did not respond to conventional MS therapy. These patients were induced to chemotherapy followed by immune injection with autologous hematopoietic stem cell transplantation (AI / aHSCT) in order to prevent further irreversible damage and preserve remaining neurological function.

	Method	Aspects detected	Positive aspects	Negative aspects
Clinical Assessment	Qualitative and quantitative tests for general body functions, cognitive and motor functions for lower limbs and fine motor functions for upper limbs.	The EDSS Scale was the parameter used in MS patients and it was found that 40% showed no change in their EDSS.	20% of patients improved. In addition, the test analyzing the motor function of the upper and lower limbs showed a trend towards improvement.	40% of patients got worse.
Visual assessment	Safety and efficacy analysis of corrected visual acuity, pupillary examination, ocular motility, alignment assessment and contrast sensitivity.	There were no significant positive changes in the parameters studied, such as color vision, vision and objective measurements (VEP and OCT) and, despite the changes reported in VEP and OCT, the patients remained with stable vision during the study.	Patients reported an improvement in the quality of their vision.	There was a decrease in the retinal nerve fiber layer in the OCT scan and an increase in the electrical conduction time of the optic nerves in the VEP analysis.
Radiological assessment	Magnetic resonance imaging at baseline and 3, 6 and 12 months after MSC injection.	90% of patients reported no change in the number of lesions in the white matter of the spinal cord. The number of enhancing lesions in the brain and spinal cord remained unchanged in 50% of patients. In addition, there was no change in the volume of the white matter lesion in 20% of the patients.	60% of patients remained with the number of lesions in the white matter of the brain unchanged; the number of lesions with enhancement in the brain and medulla decreased in 20% of patients; 10% of patients registered a decrease in the volume of the lesion in the white matter.	40% of patients had an increase in the number of lesions in the white matter of the brain; 10% of patients had an increase in the number of lesions in the white matter of the spinal cord; the number of lesions with enhancement in the brain and spinal cord increased in 30% of patients; 70% of patients had an increase in the volume of the lesion in the white matter
Inflammatory assessment	The concentration of biomarkers released by BM-MSCs was examined in 7 patients tested.	Interleukins, endothelial growth factor and monocyte chemoattractant protein-1 were detected.	Not specified.	Not specified.

Table 2: Results of the article by Dahbour *et al.*, 2017.

Source: Prepared by the authors.

The respective changes in total brain volume were calculated respectively between baseline and follow-up magnetic resonance imaging. A model was applied using two predictors: total busulfan dose and baseline volume of T1-weighted white matter lesions .

Treatment was followed by an accelerated total brain volume loss of 3.3% on average. Both the dose of busulfan and the baseline volume of the lesion were significant predictors. Atrophy progressively decreased over approximately 2.5 years. There was no evidence that edema resolution contributed to volume loss. The average long-term rate of atrophy was -0.23% per year, consistent with the expected rate of normal ageing. There was no significant correlation between the baseline EDSS scale and atrophy rates. After AI/HSCT, MS patients showed accelerated total brain atrophy, probably associated with treatment-related toxicity and degeneration of compromised tissues. During the active therapeutic trial it was noticed that atrophy eventually decreased to that expected from normal aging, suggesting that stopping inflammatory activity in MS may reduce secondary degeneration and atrophy (LEE *et al.*, 2017).

DISCUSSION

Autologous OM transplantation works by destroying the cells that attack the MS sufferer's body and by extensively renewing their immune system. There is currently a consensus on the positive changes in the immune system following the procedure. The neurological changes resulting from autologous BM transplantation depend mainly on the patient's clinical condition. The greatest effectiveness is seen in aggressive cases of MS, in young individuals, and with signs of active disease observed in the clinic and on magnetic resonance images, such as new areas of T2 lesion or gadolinium-enhancing lesions (MANCARDI *et al.*, 2017).

In general, all the articles analyzed showed that therapy based on autologous BM transplantation is relatively stable and effective. The article by Cohen *et al.* (2018) considered this therapy to be feasible, safe and tolerable, with 75% of the participants showing no relapse, while only 12.5% had a single relapse and 12.5% two relapses. The articles by Guillaume-Jugnot *et al.* (2019) and Muraro *et al.* (2017) emphasized that the best results were achieved in the long term and that post-transplant patients had high neurological progression-free survival rates.

Mancardi *et al.* (2017) confirm the results found in this review. According to the authors, in recent years, numerous studies have been published with convincing demonstrations of the efficacy of autologous BM transplantation for aggressive forms of MS. The authors emphasize that transplantation is not intended to replace existing drug therapies, but has great therapeutic value for patients with aggressive forms of the disease who do not respond to conventional treatments.

In this sense, it is understood that autologous BM transplantation is probably the most effective anti-inflammatory therapy available, and should be used when there are clear signs of inflammation and after failure to respond to first- and second-line treatments or to highly effective therapies such as alemtuzumab, natalizumab, ocrelizumab and daclizumab, but before the patient becomes seriously disabled (MANCARDI *et al.*, 2017).

A study by Boffa *et al.* (2020a) corroborates the indication for autologous BM transplantation in patients with persistent disease activity after treatment with alemtuzumab. The data found by the authors demonstrate the short--term efficacy and safety of this therapy, and all the patients studied were free of disease activity at the last post-transplant follow-up, which suggests that transplantation can be considered an effective treatment strategy for patients with persistent disease activity despite the use of alemtuzumab.

According to Boffa *et al.* (2020b) patients with aggressive relapsing-remitting MS who underwent autologous BM transplantation had an 85% chance of surviving without the risk of new inflammatory activity seen on MRI. This rate was even better than that of patients treated with alemtuzumab, which was 75%. This information corroborates the results of Lee *et al.* (2017), who observed that patients induced to chemotherapy followed by autologous OM transplantation obtained a decrease in inflammatory activity caused by MS and atrophy in the long term, maintaining the normal pattern expected during the aging process.

The EDSS scale was the evaluation criterion used in most of the articles studied, but the results varied according to each study. The article by Lee *et al.* (2017) found no significant relationship between the scale and atrophy rates; however, the articles by Sahraian *et al.* (2018) and Muraro *et al.* (2017) monitored patient assessment and found a variation between increases and decreases in the scale over the course of treatment. Sahraian *et al.* (2018) observed that the neurological asses-

sment using the EDSS scale score decreased from 0.5 to 1 point over the course of two years after transplantation, positively indicating that it is an effective therapy for treating MS.

This scale was developed by John F. Kurtzke and aims to measure the maximum functionality, limited by neurological deficits, of MS patients based on the neurological examination. It is structured into functional systems: 1. Pyramidal; 2. Cerebellar; 3. Brainstem; 4. Sensory; 5. Bowel and bladder; 6. Visual; 7. Cerebral or mental; 8. Other functions. The assessment of these systems together encompasses all the possible neurological dysfunctions caused by MS lesions. Its score is based on 10 gradations, ranging from 0 (normal) to 10 (death due to MS). The higher a patient's score on the EDSS, the greater the degree of dysfunction (KURTZKE, 1983).

Signori *et al.* (2020), in a study to assess post-transplant improvement in patients with relapsing-remitting MS and secondary progressive MS, found that almost all individuals with relapsing-remitting MS who achieved improvements maintained them during five years of follow-up, while almost all with secondary progressive MS showed a reversal of improvement. The authors concluded that the benefits of autologous BM transplantation are clearly better in patients with relapsing-remitting MS, a result that reinforces the findings of previous studies about the greater decrease in the EDSS scale score in patients with this form of MS.

With regard to the patients analyzed, the articles by Sahraian *et al*. (2018), Muraro *et al.* (2017) and Cohen *et al.* (2018) analyzed patients with relapsing-remitting MS and secondary progressive MS. Relapsing-remitting MS proved to be the most suitable for transplantation, as it is the one that achieved the best results after treatment, but the article by Sahraian *et al*. (2018) considered the most effective therapy for patients with secondary progressive MS.

Regarding mortality due to transplantation, Mancardi *et al.* (2017) state that the risk has decreased significantly in recent years due to better selection of patients eligible for treatment, in this case young patients with the relapsing-remitting form of MS and without severe disabilities. In addition, a factor associated with the decreased chances of post-transplant death is the preparation and technical conditions of the hematology and neurology centers. Sormani *et al.* (2017) cited by Boffa *et al.* (2020b) indicate that the risk of mortality in patients with aggressive MS undergoing autologous BM transplantation has fallen to 0.3% in the last decade.

The article by Dahbour *et al.* (2017) did not find any deaths or unfavorable events during the analysis, but the articles by Guillaume-Jugnot *et al.* (2019), Muraro *et al.* (2017) and Cohen *et al.* (2018) saw patients die, and in the article by Cohen *et al*. (2018), it was apparently not related to the transplant. Guillaume-Jugnot *et al.* (2019) also point out that MS patients have the lowest risk of death among patients with autoimmune diseases undergoing autologous BM transplantation.

After the transplant and the follow-up of the patients throughout the study, some points were reached differently. The article by Muraro *et al.* (2017) found that patients remained free of progressive neurological diseases five years after autologous BM transplantation. However, the article by Dahbour *et al.* (2017) obtained negative and positive points in some criteria. Regarding the clinical evaluation, it was found that most patients worsened, but in the visual evaluation, patients reported improved vision. As for the radiological assessment, most of the results showed that the number of lesions in the white matter of the brain remained unchanged and, in some cases, a decrease in spinal cord and brain lesions was observed.

In addition, the study by Lee *et al.* (2017) suggests that atrophy and secondary degeneration can be reduced by blocking inflammatory activity in MS, which corroborates the effectiveness of stabilizing the disease through the use of autologous bone marrow-derived mesenchymal stromal stem cells (BM-MSCs), proposed by the study by Dahbour *et al.* (2017). The article by Cohen *et al.* (2018) reinforces the feasibility and safety of using BM-MSCs. However, like Dahbour *et al.* (2017), there is a need for further studies to determine the efficacy of the treatment in the fight against MS.

This article contributes directly to national production on the subject, since there are few studies on the subject published in Brazil. It should be added that this research used current articles of relevance to the study, which helped to demonstrate important elements for understanding the effectiveness of autologous BM transplantation as a medical treatment for MS. However, the analyses were based on a small number of articles. Further studies are essential in order to deepen the subject and add to scientific discoveries and progress.

CONCLUSION

The treatment of MS is still the subject of much debate in the scientific community, given that some patients do not respond to conventional treatment. In this scenario, autologous OM transplantation appears as a therapeutic alternative.

Many studies on the efficacy of autologous BM transplantation are currently being carried out with promising results, showing that the majority of patients have neurological progression-free survival. This article, in general, found positive results regarding this therapy. However, despite being shown to be an alternative, the studies indicate the need for further clarification of its efficacy and safety.

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Note: This article should be written in Arial or Times font size 12, with 1.5 cm spacing between lines and justified text.

The group coordinator will send this activity via the Academic Blog, with a date set by the teachers.

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