

Selected aspects of the treatment of multiple sclerosis

(Wybrane aspekty leczenia stwardnienia rozsianego)

K Czerwińska-Mazur^{1,A,D}, M Kulesa-Mrowiecka^{1,F}, Z Kopański^{1,C,E}, J Tabak^{2,B,C},
M Mazurek^{2,B}

Abstract – The authors characterized the progress that has been made in the last decades in the treatment of multiple sclerosis. They emphasized that treatment of MS should be carried out in a continuous manner. As long as the patient feels the efficacy of the therapy or does not have any adverse effects, the treatment shall be continued. However, it should be remembered that while maintaining the individualization of therapy, not every patient responds to any form of therapy. They characterized groups of drugs selected for the specific phase of the disease. They discussed the most commonly used drugs of particular groups, they paid attention to the risk of developing symptoms. In many cases, pharmacological treatment requires support from a psychologist, psychiatrist, rehabilitation and physiotherapy. These last issues are discussed a bit more widely.

Key words - multiple sclerosis, treatment.

Streszczenie – Autorzy scharakteryzowali postęp jaki dokonał się w ostatnich dziesięcioleciach w leczeniu stwardnienia rozsianego. Podkreślili, że leczenie w SM należy prowadzić stale, w sposób ciągły. Dopóty pacjent odczuwa skuteczność terapii lub nie ma nasilonych, wykluczających to leczenie działań niepożądanych, tak długo powinien być leczony. Należy jednak pamiętać, że przy zachowaniu indywidualizacji terapii nie każdy chory odpowiada na każdą formę terapii. Scharakteryzowali grupy leków dobierane do fazy choroby. Omówili najczęściej stosowane leki poszczególnych grup, zwrócili uwagę na ryzyko rozwoju objawów. W wielu wypadkach leczenia farmakologiczne wymaga wsparcia ze strony psychologa, psychiatry oraz rehabilitacji i fizjoterapii. Te ostatnie zagadnienia omówiono nieco szerzej.

Słowa kluczowe - stwardnienie rozsiane, leczenia.

Author Affiliations:

1. Faculty of Health Sciences, Collegium Medicum, Jagiellonian University
2. Collegium Masoviense – College of Health Sciences, Żyrardów

Authors' contributions to the article:

- A. The idea and the planning of the study
- B. Gathering and listing data
- C. The data analysis and interpretation
- D. Writing the article
- E. Critical review of the article
- F. Final approval of the article

Correspondence to:

Prof. Zbigniew Kopański MD PhD, Faculty of Health Sciences, Collegium Medicum, Jagiellonian University, Piotra Michałowskiego 12 Str., PL- 31-126 Kraków, Poland, e-mail: zkopanski@o2.pl

Accepted for publication: November 30, 2018.

I. INTRODUCTION

According to many authors, since the early 1990s, there has been a steady progress in the treatment of multiple sclerosis. The first drugs of this decade were interferons and glatiramer acetate used to treat relapsing-remitting disease. Currently, it is possible to use drugs that reduce the disease activity by as much as 60%. Nowadays, drugs from the group of monoclonal antibodies have been used in the treatment. One of them is ocrelizumab, used to treat the primary progressive form (a form of the disease that had not been treated so far). This drug is effective in relapsing-remitting type, but as the only drug currently has a registration for the treatment of PPMS, which accounts for several to twenty percent of all cases of multiple sclerosis. The therapeutic efficacy of ocrelizumab has pointed to the un-

noticed before role of the immune system in the development of multiple sclerosis.

It is emphasized that treatment in MS should be carried out in a continuous manner. As long as the patient feels the effectiveness of the therapy or does not have any severe side effects, this treatment should be continued for as long as possible [1-5].

However, it should be remembered that while maintaining the individualization of therapy, not every patient responds to any form of immunological therapy. Each of these drugs works in a different mechanism, and the essence of the individual treatment is to match a patient with an effective drug. For 30% of patients, due to the mild course, effective drugs are interferons or glatiramer acetate. Some patients, however, require modern aggressive therapy. This applies mainly to the relapsing-remitting type with a large number of relapses at the very beginning and with a high risk of rapid progression of disability. [5-7]

A big problem in Poland is the fact that currently only about 26% of diagnosed patients with multiple sclerosis are treated, i.e. about 12,000. patients, while in the European Union this rate is almost twice as high and amounts to approximately 50%. In the current state of therapy in Poland, the most urgent task is to introduce changes in the treatment of the second line. This applies to the introduction of new drugs as well as the extension of the therapy time. Removing a patient from therapy as a result of the expiration of treatment in the second line may result in an increase in disease activity, i.e. relapses and active foci, or a rebound effect (after discontinuation of both one and the other linear drug II, a rapid increase may occur in disease activity). [8]

II. TREATMENT OF MULTIPLE SCLEROSIS

In the treatment of MS, four groups of drugs are used for the phase of the disease [1,5,8]:

- immunomodulatory drugs – they change the natural course of the disease, delay its development by reducing the disease relapses and their severity,
- immunosuppressive drugs – so-called emergency therapy when there is a significant deterioration of health (their effectiveness is still being investigated),
- symptomatic drugs – medicines adapted to a particular patient, prescribed by the attending physician, dedicated to alleviating the emerging symptoms,
- medicines used during the attack of the disease (most often corticosteroids) - their task is to ‘suppress’ (immunosuppression) the immune system in order to stop inflammatory processes. They are given to patients with relapsing-remitting MS after the diagnosis.

Immunomodulatory treatment is recommended primarily in the case of relapsing-remitting disease – then the therapy brings the best results. The most commonly used immunomodulatory drugs are: beta interferons, glatiramer acetate, dimethyl fumarate, natalizumab, fingolimod, teriflunomide, alemtuzumab. [9-12]

Immunosuppressive therapy is used in the case of severe, rapid relapsing-remitting MS or in a secondary progressive form. Mitoxantrone used intravenously is the most frequent in this case. The drug can give a wide range of side effects: nausea, hair loss, respiratory and urinary tract infections. [3-5]

Symptomatic pharmacological treatment is most commonly used in relation to: spasticity, dysfunction of the urinary tract, tiredness, pain, tremors, sexual dysfunctions, depression, cognitive disorders. In many cases, this type of treatment requires support from a psychologist, psychiatrist, rehabilitation and physiotherapy. [5,9,12]

Corticosteroids are most commonly used to treat acute attacks. Currently, methylprednisolone is the most commonly used one. It is administered intravenously (in a drip infusion). Depending on the severity of the relapse, methylprednisolone is administered from 3 to 5 days. Due to its good efficacy, treatment with oral corticosteroids may also be considered. In severe relapses of the disease and lack of efficacy of corticotherapy, therapeutic plasmapheresis (5 treatments) can be performed or intravenous immunoglobulins administered, especially when there are contraindications to conventional therapy [13-15].

III. REHABILITATION

Rehabilitation is generally a process aimed at improving the patient's condition and, if possible, returning to the physical condition from before the illness. Its goal is to get as little disability as possible due to illness, high independence of movement, social and mental balance. Among patients with multiple sclerosis, rehabilitation is an indispensable element of an effective treatment process. Patients with MS should be under physiotherapy at the early stages of the disease. Regardless of whether the diagnosis has already been determined or if it is probable, there are no obstacles to implement rehabilitation. The beginning of early-stage rehabilitation can prevent the patient's possible limitations and disabilities [16,17].

An improvement therapy should be common, available and carried out regularly on a continuous basis. It cannot end when the patient is discharged from a medical facility, it is important to continue the therapy later on. Rehabilitation conducted in a systematic way allows a positive influ-

ence on the patient's mental state and general well-being. The course of therapy must be comprehensive, it means that not only the physiotherapist, but the entire rehabilitation team is involved in the improvement process. It includes a physiotherapist, a main doctor, a nurse, a psychologist and a social assistant. Improvement activities should not only take into account physical rehabilitation, but also mental rehabilitation, which not only will allow the patient to fit into the new situation, but also to accept limitations and illness. Thanks to this, the patient will start to perceive the illness differently, which will have a positive impact on the whole rehabilitation process. These activities will be reflected in greater motivation and willingness to achieve more beneficial therapeutic effects [18, 19].

The most important goal for people with multiple sclerosis is to maintain their full physical and mental fitness for as long as possible. Other, secondary goals, include increasing muscle strength and preventing its loss, eliminating contractures and maintaining the full range of joint mobility, fighting spasticity, reducing the risk of balance disorders and improving motor functions lost during the disease. The other tasks posed by patients also include: regulation of physiological functions, combating the effects of immobilization, i.e. decubitus and bone decalcification, improvement of mental comfort, in some cases speech reeducation and adaptation of the patient to new living conditions. An inseparable element of the improvement process is adaptation to the activities performed daily and participation in social life, which changed during the course of illness [17,18,20,21].

Widely understood rehabilitation is an important element in the general improvement of patients. Successful therapy gives the opportunity to restore mobility and contributes to improvement in the field of social and professional rehabilitation. Thanks to the use of various methods and forms of treatment appropriately selected to the patient's condition, we prevent muscle atrophy, thus contributing to the increase of strength, endurance and muscle mass [19]. Exercises contribute to the easier flow of venous blood from the muscles and tissues towards the heart. This process leads to improved tissue trophology and increased ability of the muscles to work. Physical activity also significantly affects the maintenance of the appropriate range of movement of the joints as well as the flexibility and length of the muscle. Therapy plays a fundamental role in the functioning of the nervous system, where, through the selection of exercises, it is possible to remove coordination and balance disorders. Daily dose of exercises works against the negative effects of immobilization. An extremely important issue in the process of rehabilitation is to convince the patient about the

important role that physical exercises carried out in a continuous manner play. The only exception is a discontinuation of rehabilitation during exacerbation of symptoms and on hot days, which are often a significant hindering factor. Regardless of the patient's current condition, one should always adjust the intensity of the exercises to the endurance and individual capacity [17,18,21].

Kinesiotherapeutic methods used during treatment include PNF improvement. The PNF method is a form of improving the neuromuscular dysfunction, which is accompanied by muscle disorder. The second method used in therapy is the NDT Bobath concept. The main assumption of the mentioned method is the action aimed at renewing the patient's natural movement, improving impaired motor skills and improving the conditions for independent living. During the therapeutic procedure, techniques are used to inhibit pathologically altered movement patterns and stimulate physiological reactions. This action is possible with normalized muscle tension, i.e. one that is not pathologically altered [18, 21].

Physical exercises are supplemented with physiotherapeutic treatments. In the case of pain caused by the disease process, magnetostimulation procedures are used. One of the properties of magnetotherapy beneficial in multiple sclerosis is an increase in cerebral blood flow and stimulation of peripheral nerves. Another alternative is cold treatment, such as: air or carbon dioxide blowing, and ventricular systemic cryotherapy treatments. After applying the cooling treatments, patients should commence movement classes in the gymnasium. The treatments that affect the improvement of the patient's condition are also electrotherapy treatments, low-frequency magnetic field, tens or transdermal nerve stimulation. Thermal treatments are also applied, to which we include irradiation with a solux lamp, IR laser therapy and treatments using paraffin [17, 20-22].

IV. REFERENCES

- [1] Bevan C, Gelfand JM. therapeutic management of severe relapses in multiple sclerosis. *Curr Treat Options Neurol* 2015;17:345-51.
- [2] Kuhle J, Disanto G, Dobson R, *et al.* Conversion from clinically isolated syndrome to multiple sclerosis: a large multicentre study. *Mult Scler* 2015;21: 1013-24.
- [3] Sorensen PS. New management algorithms in multiple sclerosis. *Curr Opin Neurol* 2014;27:246-59.
- [4] Cross AH, Naismith RT. Established and novel disease-modifying treatments in multiple sclerosis. *J Int Med* 2014;275:350-63.
- [5] Hawkins CP, Wolinsky JS. Principles of treatments in multiple sclerosis. Oxford; Butterworth-Heinemann, 2017.
- [6] Rudick RA, Stuart WH, Calabresi PA, *et al.* Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. *N Engl J*

- Med 2006;354:911-23.
- [7] Ramsaransing GS, DeKeyser J. Predictive value of clinical characteristics for “benign” multiple sclerosis. *Eur J Neurol* 2007;14:885-9.
- [8] Polskie Towarzystwo Stwardnienia Rozsianego. Leczenie stwardnienia rozsianego. [online] [cited 2018 May 30] Available from: URL: https://www.ptsr.org.pl/leczenie_rzutu_choroby,351.asp
- [9] Zakrzewska-Pniewska B. Podstawy diagnostyki i leczenia stwardnienia rozsianego. Gdańsk; Via Medica, 2010.
- [10] Losy J. Stwardnienie Rozsiane. Lublin; Wydawnictwo Czelej, 2013.
- [11] Multiple Sclerosis Therapy Consensus Group. Basic and escalating immunomodulatory treatments in multiple sclerosis: Current therapeutic recommendations. *J Neurol* 2008;255:1449-63.
- [12] Bartosik-Psujek H. Algorytmy diagnostyczne i kryteria kwalifikacji do leczenia immunomodulacyjnego w stwardnieniu rozsianym. *Pol Prz Neurol* 2012;2: 76-83.
- [13] Alam SM. Methylprednisolone in multiple sclerosis: a comparison of oral with intravenous therapy at equivalent high dose. *J Neurol Neurosurg Psychiatry* 1993; 56: 1219-1220.
- [14] Barnes MP. Intravenous methylprednisolone for multiple sclerosis relapse. *J Neurol Neurosurg Psychiatry* 1985, 48: 157-159.
- [15] Barnes D. Randomized trial of oral and intravenous methylprednisolone in acute relapses of multiple sclerosis. *Lancet* 1997, 349:902-906.
- [16] Dworżańska E, Mitosek- Szewczyk K, Stelmasiak Z. Zespół zmęczenia w stwardnieniu rozsianym. *Neurol Neurochir Pol* 2009; 43: 71-76.
- [17] Cywińska- Wasilewska G, Czernicki J, Kinalski R, Krukowska J, Kwolek A, Łukasiak A, *i wsp.* Fizjoterapia w neurologii i neurochirurgii. Warszawa; Wydawnictwo Lekarskie PZWL, 2012.
- [18] Potemkowski A, Opara J. Potrzeby i możliwości rehabilitacji chorych na stwardnienie rozsiane w Polsce. *Aktualn Neurol* 2015, 15(2): 74-79.
- [19] Kowalik J. Niesprawność ruchowa, a jakość życia chorych na stwardnienie rozsiane poddanych rehabilitacji. *Probl Hig Epidemiol* 2012; 93(2): 334-340.
- [20] Antczak A, Baranowska-Bik A, Bartosik-Psujek H, Białecka M, Bik W, Członkowska A, *i wsp.* Neurologia. Warszawa; Medical Tribune, 2015.
- [21] Pasek J, Opara J, Pasek T, Manierak- Pasek A, Sieroń A. Rehabilitacja w stwardnieniu rozsianym- wyzwanie współczesnej medycyny. *Aktualn Neurol* 2009; 9(4): 272-276.
- [22] Cholewa J, Gorzkowska A, Nawrocka A, Cholewa J. Jakość życia osób z chorobą Parkinsona w kontekście pracy zawodowej i rehabilitacji ruchowej. *Med Pr* 2017; 68(6): 725-734.