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Adherence to Therapeutic Recommendations in Patients Suffering from Multiple Sclerosis

Przestrzeganie zaleceń terapeutycznych u pacjentów chorych na stwardnienie rozsiane

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Abstract

Introduction. Multiple sclerosis is a chronic, inflammatory, immune demyelinating disease of the central nervous system. The effectiveness of MS treatment depends primarily on the effectiveness of drugs and the patient's compliance with the principles of therapy.

Aim. The main aim of the study was to assess the level of adherence to therapeutic recommendations in patients with multiple sclerosis.

Material and Methods. The research was carried out at the Department of Neurology and Clinical Neuroimmunology of the Regional Specialist Hospital in Grudziądz. On average 165 patients suffering from multiple sclerosis were qualified for the study. The study was conducted using the method of diagnostic survey. The variables were measured using the proprietary questionnaire containing sociodemographic and medical data and the standardized adherence scale in chronic diseases (ACDS).

Results. The analysis of own research showed that patients with high-level multiple sclerosis adhere to the therapeutic recommendations ($p=0.001$). The study group reported the fatigue syndrome at all ACDS levels ($p=0.002$). There was no relationship between the occurrence of adverse effects of pharmacotherapy and the level of compliance with therapeutic recommendations ($p>0.05$).

Conclusions. It was found that the level of adherence to therapeutic recommendations in patients suffering from multiple sclerosis in the study group remained at a high level. (JNPN 2020;9(3):103–107)

Key Words: adherence, multiple sclerosis, therapeutic recommendations

Streszczenie

Wstęp. Stwardnienie rozsiane jest przewlekłą, zapalną chorobą demielinizacyjną ośrodkowego układu nerwowego o podłożu immunologicznym. Skuteczność leczenia SM zależy przede wszystkim od efektywności działania leków oraz związanej z tym przestrzegania zasad terapii przez pacjenta.

Cel. Głównym celem badań była ocena poziomu przestrzegania zaleceń terapeutycznych u pacjentów chorych na stwardnienie rozsiane.

Materiał i metody. Badania przeprowadzono w Oddziale Neurologii i Neuroimmunologii Klinicznej Regionalnego Szpitala Specjalistycznego w Grudziądzu. Do badań zakwalifikowano 165 pacjentów chorujących na stwardnienie rozsiane. Badanie przeprowadzono za pomocą metody sondażu diagnostycznego. Do pomiaru zmiennych wykorzystano autorski kwestionariusz ankiety zawierający dane socjodemograficzne i medyczne oraz standaryzowaną skalę adherence w chorobach przewlekłych (ACDS).

Wyniki. Analiza badań własnych wykazała, że pacjenci ze stwardnieniem rozsianym na poziomie wysokim przestrzegają zaleceń terapeutycznych ($p=0,001$). Badana grupa na wszystkich poziomach w skali ACDS zgłaszała występowanie zespołu zmęczenia ($p=0,002$). Nie stwierdzono związku pomiędzy występowaniem działań niepożądanych stosowanej farmakoterapii, a poziomem przestrzegania zaleceń terapeutycznych ($p>0,05$).

Wnioski. Stwierdzono że, poziom przestrzegania zaleceń terapeutycznych u pacjentów chorych na stwardnienie rozsiane w badanej grupie utrzymuje się na wysokim poziomie. (PNN 2020;9(3):103–107)

Słowa kluczowe: przestrzeganie, stwardnienie rozsiane, zalecenia terapeutyczne

Introduction

Adherence to therapeutic recommendations is synonymous with the English term adherence. According to Brian Haynes, this is “the extent to which the patient’s behaviour in relations to taking medications, adherence to diet and lifestyle modifications remains consistent with the patient’s accepted medical recommendations” [1].

Multiple sclerosis (SM) is a chronic, idiopathic, immune-mediated inflammatory demyelinating disease of the central nervous system, in which an abnormal response of the immune system damages myelin and axons, leading to permanent motor disability. Long-term immunomodulating therapy in multiple sclerosis prevents relapses and delays the progression of the disease. Earlier studies have shown that the number of patients with multiple sclerosis who adhere to therapeutic recommendations ranges from 49% to 93% [2].

Many of the well-documented studies conducted around the world indicate that patients fail to adhere to therapy recommendations mainly due to side effects and ineffectiveness of treatment, which in turn leads to a deterioration of control over the course of the disease. O’Rourke and Hutchinson [3] proves that during the first year of treatment with interferons β 1b and β 1a, drug tolerance was the decisive factor in maintaining therapy. Similar observations were made by Treadaway et al. [4], which showed that patients discontinuing treatment are three times more likely to be uncertain about the effectiveness of their treatment. The most common reason for a missed dose was that the patient had forgotten to take it. Some patients also reported fear of injections.

In Poland, only one study has been conducted and published so far, which examined the degree of compliance with therapeutic recommendations in patients with multiple sclerosis treated with first-line injectable immunomodulating drugs, without assessing oral drugs and second-line drugs [5]. Therefore, our own research was to answer the question of what is the level of compliance with therapeutic recommendations among patients from multiple sclerosis treated with drugs modifying the course of the first and second line disease.

The main aim of the study was to assess the level of adherence to therapeutic recommendations in patients suffering from multiple sclerosis.

Material and Methods

The research was carried out in the Department of Neurology and Clinical Neuroimmunology of the Regional Specialist Hospital in Grudziądz. On average 165 patients suffering from multiple sclerosis were qualified for the study. Among the surveyed people, 124 people (75.2%) were women, 41 people were men (24.8%). The age of the respondents ranged from 18 to 66 years of age. The mean age of the patients was 39.6 years. The vast majority of respondents lived in a city with more than 100,000 inhabitants 37.2% (N=61). A comparable group were people living in towns with less than 100,000 inhabitants 31.7% (N=52) and in villages 31.1% (N=51).

The study was conducted using the method of diagnostic survey. The variables were measured using the proprietary questionnaire containing sociodemographic and medical data and the standardized adherence scale in chronic diseases (ACDS).

The questionnaire was anonymous and contained questions concerning, among others: sociodemographic factors, current pharmacotherapy, duration of the disease, duration of treatment, occurrence of side effects of the treatment used, the occurrence of the fatigue syndrome.

The scale of adherence in chronic diseases (ACDS) is a new tool developed in Poland by Professor Aldona Kubica [6]. The scale is used to test the implementation of the therapeutic plan by patients with chronic diseases. The scale contains 7 questions with proposed sets of 5 answers to each question. The questions related to the behaviours that directly determine adherence (questions 1–5) and to situations and views that may indirectly affect adherence (questions 6–7). The ACDS scale is intended for testing adults treated for chronic diseases. This tool is intended not only to reflect the actual implementation of the therapeutic plan in the field of pharmacotherapy, but also to indicate the mechanisms determining the adherence to patients’ therapeutic recommendations. The results may be helpful in taking steps to improve the regularity of medication intake in clinical practice. For the purposes of the research, the division of patients was proposed according to the established criteria: result ≤ 20 — low level, 21–26 — medium level ≥ 27 — high level.

All statistical calculations were performed using the StatSoft. Inc. statistical package (2014). STATISTICA (data analysis software system). version 12.0. www.statsoft.com and the Excel spreadsheet. In all calculations, the level of significance was set at $p=0.05$.

The research was approved by the Bioethical Committee of the Nicolaus Copernicus University in Toruń at the Ludwik Rydygier Collegium Medicum in Bydgoszcz.

Results

When assessing the implementation of the therapeutic adherence plan by patients, made using the ACDS scale (Table 1), it can be noted that 113 respondents (68.5%) obtained a score of ≥ 27 , which means a high level of compliance with therapeutic recommendations among patients with multiple sclerosis. The average level of compliance with therapeutic recommendations concerns 45 (27.3%) of the respondents, the low level of compliance with therapeutic recommendations among patients with multiple sclerosis concerns only 4.2% (N=7) of the respondents. The distribution of patients

with particular values of the ACDS scale differed in a statistically significant way ($p=0.0001$), which means that patients show a high level of compliance with therapeutic recommendations.

Based on the results, the responses to the questionnaire (Table 2) were analysed. Positive responses to the question “Have you ever missed the recommended medication?” in relation to the ACDS scale category (low, medium and high level) are respectively 14.3% vs. 42.2% vs. 30.1% ($p=0.1939$). The respondents answered positively to the question “Do you have a fatigue syndrome?” in relation to the ACDS scale category (low, medium and high level) are, respectively, 85.7% vs. 93.3% vs. 67.3%; the distribution of answers differed in a statistically significant way ($p=0.0023$). Positive responses to the question “Have you had pessimistic thoughts?” in terms of the ACDS scale (low, medium and high level) are, respectively, 42.9% vs. 15.6% vs. 15.9% ($p=0.1755$). Answers to the question “Have you ever had a lack of willingness to do anything?” in relation to the ACDS scale (low, medium and high level), 28.6% vs. 48.9% vs. 38.1% ($p=0.3668$) responded positively, respectively. When asked “Have you had any sleep disorders?” in relation to the ACDS scale (low, medium and high level),

Table 1. Level of adherence to treatment recommendations according to the ACDS scale

| ACDS scale | Total (N=165) | P-value |
|------------------------|---------------|---------|
| ACDS value | | 0.0001 |
| ≤ 20 — low level | 7 (4.2%) | |
| 21–26 — average level | 45 (27.3%) | |
| ≥ 27 — high level | 113 (68.5%) | |

Chi-square test

Table 2. ACDS and responses to survey questions

| Survey question | ACDS | | | P-value |
|--|-----------|------------|------------|---------|
| | Low | Average | High | |
| Have you ever missed your medication intake? | | | | 0.1939 |
| Yes | 1 (14.3%) | 19 (42.2%) | 34 (30.1%) | |
| No | 6 (85.7%) | 26 (57.8%) | 79 (69.9%) | |
| Do you have fatigue syndrome? | | | | 0.0023 |
| Yes | 6 (85.7%) | 42 (93.3%) | 76 (67.3%) | |
| No | 1 (14.3%) | 3 (6.7%) | 37 (32.7%) | |
| Do you have pessimistic thoughts? | | | | 0.1755 |
| Yes | 3 (42.9%) | 7 (15.6%) | 18 (15.9%) | |
| No | 4 (57.1%) | 38 (84.4%) | 95 (84.1%) | |
| Do you experience a lack of desire to do anything? | | | | 0.3668 |
| Yes | 2 (28.6%) | 22 (48.9%) | 43 (38.1%) | |
| No | 5 (71.4%) | 23 (51.1%) | 70 (61.9%) | |
| Do you have any sleep or appetite disorders? | | | | 0.2983 |
| Yes | 3 (42.9%) | 21 (46.7%) | 38 (33.6%) | |
| No | 4 (57.1%) | 24 (53.3%) | 75 (66.4%) | |
| Do you experience sadness? | | | | 0.2369 |
| Yes | 3 (42.9%) | 7 (15.6%) | 25 (22.1%) | |
| No | 4 (57.1%) | 38 (84.4%) | 88 (77.9%) | |
| Do you have difficulty concentrating your attention? | | | | 0.0947 |
| Yes | 5 (71.4%) | 17 (37.8%) | 36 (31.9%) | |
| No | 2 (28.6%) | 28 (62.2%) | 77 (68.1%) | |

Chi-square test

positive responses are, respectively, 42.9% vs. 46.7% vs. 33.6% ($p=0.2983$). Positive responses to the question “Have you experienced any sadness?” in relation to the ACDS scale (low, medium and high level) are, respectively, 42.9% vs. 15.6% vs. 22.1% ($p=0.2369$). Positive responses to the question “Have you had difficulty concentrating?” in relation to the ACDS scale (low, medium and high level) are, respectively, 71.4% vs. 37.8% vs. 31.9% ($p=0.0947$).

Among the reasons why patients did not take the recommended dose of the drug (Table 3), the most frequently mentioned were forgetfulness (19.8%), other

Table 3. Adverse reactions and reasons for not taking the drug

| Reason for not taking the drug | Yes | No | P-value |
|----------------------------------|------------|-----------|---------|
| Departure | 2 (1.6%) | 1 (2.6%) | 0.6899 |
| Forgetfulness | 25 (19.8%) | 4 (10.3%) | 0.1694 |
| Disease/surgery | 10 (7.9%) | 1 (2.6%) | 0.2399 |
| Side effects of the drug/fatigue | 5 (4.0%) | 0 (0.0%) | 0.2065 |
| Other | 4 (3.2%) | 1 (2.6%) | 0.8459 |

Chi-square test

disease or surgery (7.9%), side effects of the applied therapy and treatment fatigue (4%), The rarest reported reason for not taking a drug dose was the departure of the patient — 1.6%. There was no statistically significant relationship between the reason for not taking the drug and the occurrence of adverse events ($p>0.05$).

Discussion

Adherence to therapeutic recommendations in a chronic disease, which is undoubtedly multiple sclerosis, is the key to effective therapy and a challenge for the entire therapeutic team.

An analysis of our own research shows that 68.5% of MS patients comply with treatment recommendations, which, according to previous studies, is not even the optimal level reported by the World Health Organization (WHO). Patients who do not comply with therapeutic recommendations in the studied group constitute only 4.2%. The results of the survey of the social campaign conducted in Poland “MS — fight for yourself” in 2015 show that 55% of respondents admitted that they had missed the drug under the first-line drug therapy [7]. Until 2017, no study evaluating the degree of compliance with therapeutic recommendations in patients with multiple sclerosis treated with immunomodulation was conducted and published in Poland.

Kołtuniuk and Rosińczuk [5] undertook such a task and conducted a study in four centres in Wrocław. The results of their research show that 76.5% of the studied patients comply with the therapeutic recommendations, which is also confirmed in the results of my work and the results of other researchers.

Recent studies conducted worldwide among patients with MS have shown that the treatment adherence population ranges from 49% to 93%. Studies on treatment adherence and factors leading to discontinuation of treatment in patients with multiple sclerosis are mainly available in the English-language literature. Devonshire et al. [8] in 2006 published the Global Adherence Program (GAP) for 2,646 patients with multiple sclerosis in 179 facilities, in 22 countries, where 25.3% of patients were found to be non-adherent. Comparing the group in my study with the GAP study, where it accounted for only 165 patients, the group of people who did not comply with the therapeutic recommendations is relatively low (4.2%). This difference is probably due to the fact that Poland has limited access to immunomodulating treatment.

In the latest meta-analysis by Giovannoni and colleagues from 2015, who analysed the data on adherence to treatment from 50 randomized trials, they observed that 17–36% of patients did not follow the recommendations [9]. The results of 24 studies published in 2001–2011 by Menzin et al. show that adherence to therapeutic recommendations in MS patients ranges from 41 to 88% [10]. The results of my study showed that patients who did not comply with the therapeutic recommendations more often indicated difficulties in concentration, which is caused by impaired cognitive functions. Many authors, such as Benedict et al., Higginson et al or Rao et al., also talk about cognitive disorders as the cause of worse functioning of patients [11–13]. It becomes logical to suppose that patients with cognitive impairment will not follow treatment recommendations because the main reason will be not taking the drug due to forgetfulness. Another reason may also be that the injection site rotation has been forgotten, and therefore the risk of injection site adverse reactions is increased, so this group of patients will report more side effects at the injection site.

Among the studied patients, the most common reason for not taking the recommended drug was forgetfulness (19.8%), another reason was surgery, another included disease, side effects of the drug used, or fatigue with therapy — only 4% of respondents indicated this. Arroyo et al. [14] and di Battista et al. [15] also mention similar conclusions regarding the forgotten drug dose as the main cause of non-compliance. Treadway also showed in the observations that in 58% of patients the main reason for not taking the drug was forgetfulness [4]. Costello et al. listed the key factors of non-compliance

with therapeutic recommendations, which also include forgetfulness, fear of injection, side effects of the applied therapy, and fatigue with therapy. The aforementioned GAP analysis also confirms this factor as the cause of non-adherence to therapeutic recommendations [8,16].

Conclusions

It was found that at the level of adherence to therapeutic recommendations in patients suffering from multiple sclerosis in the study group remained at a high level.

Implications for Nursing Practice

A nurse caring for a patient with multiple sclerosis is at the centre of patient care, cooperating with a doctor, physiotherapist, psychologist and other members of the therapeutic team. It is the MS nurse who provides constant support and education to patients from the moment of diagnosis. This mainly concerns realistic treatment expectations, training in the use of the auto-injector, as well as advice on what to do in case of side effects. It is important to maintain constant contact with the patient throughout the course of treatment, even by telephone, so as not to overlook the signs of, for example, fatigue with treatment. Due to the introduction of newer and newer drugs into the treatment of multiple sclerosis, the need for specialist professional training is increasing, so that the nurse caring for a patient with multiple sclerosis is a doctor's partner in the therapy.

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