SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS IN RUSSIA: PROBLEMS AND NEEDS OF PATIENTS, ASSESSMENT OF THE QUALITY OF MEDICAL CARE THROUGH THE EYES OF PATIENTS AND SPECIALISTS

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The article discusses the most unfavorable course of multiple sclerosis — the secondary progressive form. In the course of the study, conducted by a questionnaire survey of patients with secondary progressive multiple sclerosis and specialists from multiple sclerosis centers from 15 regions of Russia, medical, labor and other characteristics of patients, their problems and needs, subjective attitude to the effectiveness of therapy and rehabilitation were clarified. The main, according to doctors, defects in the organization of medical care for patients with secondary progressive multiple sclerosis have been identified. In conclusion, it was concluded that there is a significant variability in the social status and living conditions of patients with secondary progressive multiple sclerosis. The authors consider the registration in the Russian Federation of highly effective drugs for the treatment of patients with secondary progressive multiple sclerosis to be one of the most important measures.

Key words: multiple sclerosis, secondary progressive, social activity, treatment of secondary progressive multiple sclerosis, disease-modifying therapy

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Compliance with the ethical standards: this study was approved by the Ethics Committee of the Yaroslavl State Medical University of the Ministry of Health of Russia (minutes #21 of February 8, 2018). Each participant signed and submitted the voluntary informed consent form. Adult participants filled out questionnaires voluntarily. The conducted study does not endanger the participants and complies with the biomedical ethics requirements.

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ВТОРИЧНО-ПРОГРЕССИРУЮЩИЙ РАССЕЯННЫЙ СКЛЕРОЗ В РОССИИ: ПРОБЛЕМЫ И ПОТРЕБНОСТИ ПАЦИЕНТОВ, ОЦЕНКА КАЧЕСТВА ОКАЗАНИЯ МЕДИЦИНСКОЙ ПОМОЩИ ГЛАЗАМИ ПАЦИЕНТОВ И СПЕЦИАЛИСТОВ

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В статье обсуждается наиболее неблагоприятный тип течения рассеянного склероза — вторично-прогрессирующая форма. В ходе исследования, проведенного методом анкетного опроса пациентов с вторично-прогрессирующим рассеянным склерозом и специалистов центров рассеянного склероза из 15 регионов России, выяснены медицинские, трудовые и другие характеристики пациентов, их проблемы и потребности, субъективное отношение к эффективности терапии и реабилитации. Выявлены основные, по мнению врачей, дефекты организации оказания медицинской помощи пациентам с вторично-прогрессирующим рассеянным склерозом. В заключение сделан вывод о наличии значительной вариабельности социального статуса и условий жизни пациентов с вторично-прогрессирующим рассеянным склерозом. Одним из наиболее важных мероприятий авторы считают регистрацию в РФ высокоэффективных средств для терапии пациентов с вторично-прогрессирующим рассеянным склерозом.

Ключевые слова: рассеянный склероз, вторично прогрессирующий, социальная активность, лечение ВПРС, ПИТРС

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease the etiology of which is multifactorial. MS triggers a set of autoimmune and neurodegenerative processes that damage central nervous system and lead to significant neurological deficit and disability already at the early stages of the development of the disease [1]. It is the most widely

Table 1. Interviewed patients by region

Region	Number of people	Share,%
Moscow	36	7,2
Moscow region	28	5,6
Saint Petersburg	29	5,8
Leningrad region	25	5,0
Volgograd region	33	6,6
Republic of Tatarstan	35	7,0
Novosibirsk region	33	6,6
Perm region	33	6,6
Rostov Region	30	6,0
Samara Region	45	9,0
Tomsk region	33	6,6
Tyumen region	34	6,8
Ulyanovsk region	41	8,2
Republic of Bashkortostan	32	6,4
Chelyabinsk region	33	6,6
Total	500	100,0

spread demyelinating disease: worldwide, there are about 2.5 million people diagnosed with MS, and in Russia the number is approximately 200 thousand [2, 3]. A significant proportion of MS patients are young people of working age; 15 years from the onset, 50% of them have confirmed disability of the 2nd degree, and over 20 years with MS typically translate into a disability of the 1st degree [4]. At the later stages of the disease, patients lose the ability to support themselves independently in routine daily activities and thus need constant support from relatives and social workers, which adds to the high socioeconomic significance of MS.

Conventionally, there are three types of MS distinguished: primary progressive MS (PPMS), which is diagnosed in 10–15% of cases; relapsing-remitting MS (RRMS); and secondary progressive MS (SPMS) [5]. Same as the general prevalence of the disease, its prevalent type is region-dependent. As of May 8 2018, the Russian Register of CNS Demyelinating Diseases included 1188 patients, 85.8% of whom had RRMS, 1.9% had PPMS and 12.3% had SPMS. The ratio of MS types can vary significantly region to region. For example, in the city of Ufa, of the total number of MS patients 15% have RRMS, 3.5% are affected by PPMS and 81.5% have SPMS, while in the rest of Russia, in USA and the EU countries the share of patients diagnosed with SPMS ranges from 12 to 39% [6]. In three-quarters of RRMS patients the disease progresses into SPMS, but both patients and medical professionals try to avoid formal registration of the SPMS case as long as possible, since most MS disease modifying drugs (MS DMDs) prove ineffective against SPMS [7, 8, 9]. Poor therapeutic options available for SPMS lead to a more serious prognosis for RRMS course [10, 11].

Thus, out of 200 thousand MS patients currently registered in Russia, approximately 25 thousand have SPMS, with 127.5 thousand expected to join them after their RRMS progresses into SPMS. The ethical importance of studies investigating SPMS is high: the patients are of the working age, their social well-being declines sharply because of the disease, most of them acquire confirmed disabilities, the prognosis is typically unfavorable and there are no effective therapies against the disease available at the moment. The high social and economic significance of the SPMS problem supports the relevance of research efforts aimed at finding solutions thereto.

MATERIALS AND METHODS

The purpose of this work was to study the status of health and the living conditions of SPMS patients and to evaluate the efficacy of SPMS therapies and the goals currently seen as primary for them. The study was conducted by the All-Russian Public Organization of Disabled People with Multiple Sclerosis and supported by the Social Mechanics Center for Humanitarian Technologies and Research. The research method selected for the study involved questionnaires SPMS patients (formally established diagnosis) and neurologists specializing in MS were asked to fill out. The data collection period spanned from May 1 to October 1, 2020. All in all, 500 SPMS patients and 51 neurologist from 15 regions of Russia took part in the study. The minimum number of interviewed patients in a region was 25 (Leningrad region), the maximum — 45 (Samara region). The sample included patients that were available for filling out the questionnaires. The data from the filled out questionnaires were processed with IBM SPSS Statistics 26 statistical software. (Table 1)

RESULTS

General data. Two-thirds of the SPMS patients who participated in the study were female, and 73% of the participants were 40 years old or older (middle age and advanced age group). Most of the patients live in a family, 67.2% — with a partner; only 9% of the participants live alone. Over two-thirds of the participating patients (76.2%) have children: 43.2% have one child, 25% have two, 5.7% of patients have more than two children; the children of 30.6% of the respondents are minors. The level of education of SPMS patients is high: 52.7% of them graduated from a higher education establishment or studied there, 35.6% finished vocational schools. The participants had a long work history and high professional status before the disease, but currently most of them (71.6%) are unemployed because of the disability. (Diagram 1)

Duration of the disease and level of disability. Most of the SPMS patients participating in the study (79%) have had MS for over 8 years. Almost a quarter of them (23.4%) were diagnosed with SPMS 2–3 years ago, 24.4% first heard the diagnosis 4–6 years ago and 26% of the patients surveyed have been living with SPMS for over 7 years, while 17.6% received the updated diagnosis in the last year.

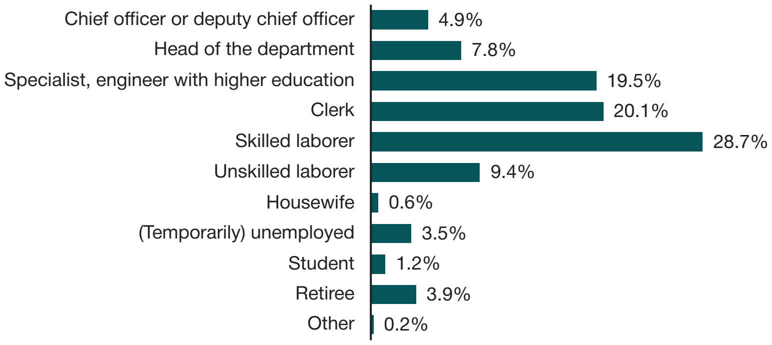

Diagram 1. Professional status of patients before the disease

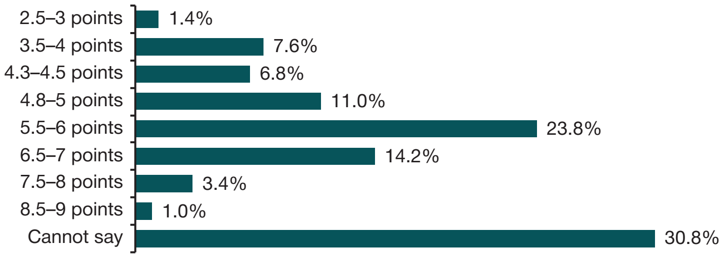

Diagram 2. SPMS patients about their EDSS scores

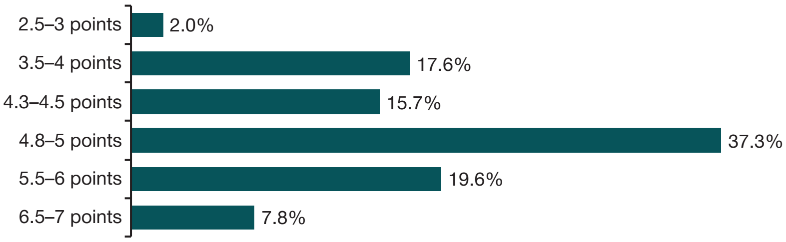

Diagram 3. Score estimated by neurologists for patients when establishing the SPMS diagnosis

The rate of manifestation of the symptoms of secondary progressive multiple sclerosis differs from patient to patient. For 32% of the participating patients, these symptoms became obvious within the first 3 years from the onset. In 20% of the respondents MS did not progress for the first 4–6 years of life with the disease. Multiple sclerosis did not develop further for 7–10 years in 28.4% of the participants, and about 20% have been living without SPMS making itself evident for over 10 years, which is a considerable period of time.

Official confirmation of disability has been given to 92.2% of the surveyed SPMS patients: 19% of them have disability of the 1st degree, 48.3% — 2nd degree disability and 25% belong to the group with disability of the 3rd degree. Typically, SPMS patients score 4.8–7 points on the EDSS scale (49% of the respondents), with 5.5–6 points being the most common result (23.8%). Patients with SPMS do not always monitor the formal parameters in assessing their condition: almost a third of the respondents (30.8%) found it difficult to answer the question about their EDSS score. Over half of participating patients (54.6%) have had the disability status for more than 7 years, 23.6% of the respondents have been officially disabled for less than 3 years and 21.8% received the formal confirmation of their disability from 4 to 6 years ago. (Diagram 2, Diagram 3.)

Self-perceived health and complaints. The majority of SPMS patients believe their health has deteriorated over the past year. The overall share of negative opinions was more than twice as great as the joint share of neutral and positive opinions (68.8% against 28.4%) However, with this many participating SPMS patients evaluating their health negatively, the share of those that stated lack of exacerbations over the past two years is relatively high: 37.4%. Among the participants that reported such incident 27.8% had one exacerbation, 16.5% had two exacerbations and 18.2% had three or more.

The symptoms that are the source of discomfort for the vast majority of SPMS patients are hindered movement and communication abilities (specific to activities outside the home), balance and gait disturbances, difficulties in moving around the house and doing household chores, fatigue and lack of energy. Over 55% of the respondents claimed to suffer manifestations of these symptoms constantly or frequently.

The symptoms that cause inconvenience to a significant number of SPMS patients have to do with individual manifestations: they find it difficult to concentrate, their urination and bowel functions are impaired, they feel dizzy; 35–50% of patients experience such symptoms constantly or often.

The list of occasional SPMS symptoms includes memory impairment, blurred vision, discomfort felt in the body, conditions like anxiety, depression and melancholy, irritability. Thirty percent of the respondents stated that they suffer manifestations of these symptoms often, 20–30% marked them as symptoms manifesting from time to time. The less common symptoms are annoyance, tearfulness, awkwardness in the presence of others and onset of depression when looked at by other people, as well as a sense of injustice. Over 50% of the participating patients have noted that these conditions are rare or unfamiliar to them. Table 2 contains answers to the question about the most disturbing manifestations of MS. (Table 2, Diagram 4.)

Table 2. Most discomforting symptoms

Complaint	Mentioned by	Complaint	Mentioned by
Ataxia	29	Nausea	1
Restricted mobility	52	Weakness, malaise	18
Balance disorder	61	Fatigue	13
Gait disturbance	65	Burning in the body	1
Weakness in the legs, dragging	53	Dizziness	29
Muscle spasticity	15	Headaches	8
Stiffness, heavy legs	13	Head numbness	1
Leg pain	10	Blocked ears	1
Leg parasthesia	9	Visual impairment	21
Leg cramps	4	Diplopia	3
Lameness	2	Rippled sight	1
Weak arms	19	Attention, memory disorders	19
Tremor	13	Irritability	4
Sensory disturbances in the hands	11	Reduced emotional background	3
Hand movement disorders	6	Anxiety	2
Difficulties with routine daily activities	4	Apathy	1
Urination disorder	64	Difficulties in communication	1
Pelvic disorders	24	Tearfulness	1
Bowel dysfunction	12	Speech disorders	6
Swallowing disorders	2	Pain in different parts of the back	4

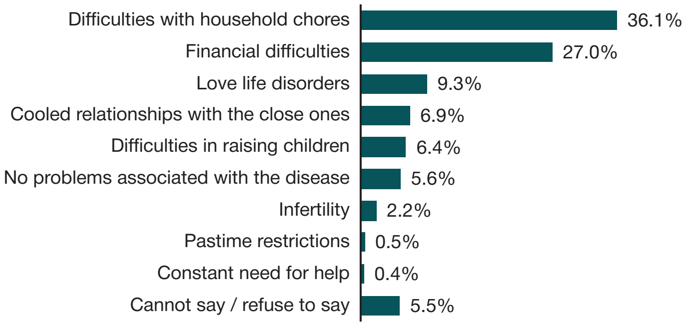

Diagram 4. Difficulties in family life caused by the disease

Living conditions of SPMS patients. As established by this study, 55% of patients with SPMS need help at home with housework and routine daily activities. Of the respondents that stated need for assistance at home, 81.5% receive help from their circle and 18.5% do not have a helper. Immediate family remains the main source of assistance in everyday life for SPMS patients: 74.8% of those who need such support receive it from their relatives. Often, the associated burden carried by the family members has no negative effect on their work. The majority of respondents (76.5%) mentioned that their relatives did not have to take a vacation, change their schedule or employment.

Most SPMS patients also receive psychological support from the family, with 67.3% of respondents mentioning family members trying to alleviate their condition, help, and another 21% noting a sympathetic attitude towards themselves. The proportion of those who say that the diagnosis has made their relations with the loved ones cooler is 7%. According to the patients, problems in the family are more often associated with mundane and material reasons and not with the psychological peculiarities of perception of the disease by the relatives.

The needs of patients with SPMS. The survey revealed some of the most pressing needs of patients. Innovative (effective) therapies, improved medical care, free drugs and monetary support were mentioned by 38–48% of the respondents. The second set of needs includes social aspects associated with belonging and reintegration: patients want to feel like full members of society, enjoy barrier-free environment and attention from others (28% of answers for each item). The third place in the rating of needs of SPMS patients was given to support and assistance, specifically, technical aids facilitating routine daily activities, movement and independent obtaining of information, as well as needs associated with timely consultations with legal/medical professionals and help with household chores (19–24% of answers). The availability of rehabilitation equipment to SPMS patients cannot be considered sufficient. Only 26–30% of the respondents have walking frames and wheelchairs, 23.6% have canes and 22% have diapers. There are handrails in the apartments of 13.8% of the participants and only 2.6% have special arms that allow unassisted activities in the kitchen. Handrails for the apartment were mentioned by 19.8% of the respondents as the equipment they need to buy; 19% did not have exercise therapy equipment but needed it; 13% stated the need for supporting arms in the kitchen to function there without assistance; 7.6% of the participants needed special shoes and 7.6% — diapers.

Eighteen percent of the respondents need professional retraining and employment. These are the patients who want to work and earn money but need help at the initial stage of retraining.

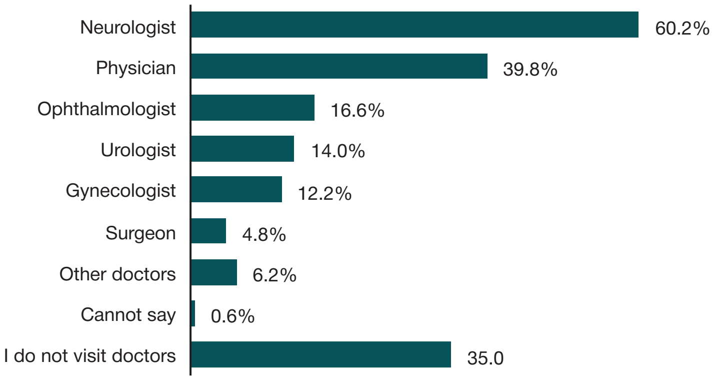

Diagram 5. Clinic doctors visited by SPMS patients

SPMS diagnosis criteria — a survey of specialists. The promptness of clarification of the diagnosis and change of therapy largely determine the success of all subsequent actions and suppression of progression of the disease. Manifestation of symptoms signaling of its development call for dynamic monitoring and timely assessment of the condition of patients. The change of the type of MS and its transition from RRMS to the progressive form is a gradual process. Clarifying the diagnosis, the neurologist takes into account patient's sensations and complaints, as well as the objective rise of severity/frequency of clinical manifestations of the disease.

Diagnosing SPMS or escalating the previous diagnosis to this type of MS, neurologists look at the increasing EDSS score registered outside of exacerbations: this criterion was mentioned by absolutely all the doctors who participated in the survey. Another phenomenon looked for when diagnosing SPMS is the disappearance of obvious exacerbations against the background of deteriorating motor activity (74% of doctors surveyed factor this criterion in when establishing the diagnosis). Repeated poor recovery after pulse therapy is the indicator taken into account somewhat less frequently: 38% of the doctors who participated in the survey pointed to this criterion. Patient complaints about cognitive or motor impairments and increased fatigue, as well as lack of therapy-induced alleviation, are not considered crucial in diagnosis clarification: only 26% and 20% of doctors surveyed, respectively, mentioned them.

The time it takes to diagnose a person with SPMS is perceived more or less similarly by medical professionals and patients. In most cases (75%), this period does not exceed 12 months. Basically, the time between manifestation of the symptoms of progression to the diagnosis can be 6 to 12 months, as stated by 38% of the interviewed patients and 42.9% of doctors, or 4 to 6 months, according to 27.3% of patients and 26.5% of neurologists. In almost a quarter of cases it may take over a year to clarify the MS diagnosis (pointed out by 24.7% of the participating patients and 24.5% of doctors). Late diagnosing of SPMS is a rare or relatively rare situation, as stated by 29.4% and 49% of the interviewed medical professionals, respectively. However, 21.6% of neurologists called this situation common. These opinions prove that improvement of the SPMS diagnosis clarification method is still an urgent matter.

The problem of late diagnosing of SPMS, according to the medical professionals surveyed, is primarily associated with the lack of clear criteria describing this disease and differentiating it from the current chronic condition of the patient (according to 65% of the respondents), as well as with the lack of SPMS therapy options (according to 56.9% of the interviewed doctors). Neurologists in polyclinics fail to focus on the problem of secondary progression of MS (according to 41.2% of the respondents), which complicates SPMS diagnosing, as does illiteracy of the patients themselves, who visit their doctors with symptoms of regression later than they should have (33% of respondents). Unavailability of equipment and lack of SPMS diagnosing methods are the reasons for late identification of the diseases that were mentioned by 19.6% of the doctors surveyed.

According to the medical professionals, MS patients should have certain skills in assessing their own condition and monitoring symptoms in order to contact a doctor in a timely manner to adjust therapy. Ignorance of patients makes the time to diagnosis even longer, which adds to the already high urgency of educational work among patients and their involvement in "patient schools" and other projects of this kind.

Outpatient care. Less than half of the patients undergo regular examinations at the place of residence (44.2% of the respondents). For 17.5%, the only reason to go to the clinic is exacerbation. Every third person diagnosed with SPMS does not visit the clinic (35.3% of the respondents), and only 7.7% of such patients skip on that activity for health reasons. The doctors SPMS primarily seek assistance of in the clinics are neurologists (60.2% of respondents) and, less often, therapists (39.8%). Up to 16% of respondents consult other medical professionals. (Diagram 5.)

The frequency of visits of SPMS patients to medical professionals depends on their area of expertise. Gynecologists, surgeons, ophthalmologists, urologists are seen by such patients one or two times a year. Neurologists and physicians receive SPMS patients somewhat more often: 33–35% of the respondents said they paid visits to these medical doctors one or two times, but another 33–35% mentioned three or four visits a year. Another third of those who go to the clinic (31%) visit the mentioned medical professionals more than 4 times a year, with 11.5% of the respondents paying visits to their neurologists every month and 13.9% of the participating patients seeing their physicians as often.

A quarter of the respondents do not turn to a doctor specializing in the relevant field of medicine even when their condition worsens. Among SPMS patients, the main reason for refusal to seek assistance is the handicap on their ability to move. Over 40% of the participants that do not visit physicians noted that it was physically difficult for them to get to the clinic. Among other reasons behind refusal to seek medical assistance are the difficulties peculiar to the medical establishments, including the complexity of obtaining an appointment note (26.5%), long waiting time (long queues of patients in the clinic) (25.3%), lack of a neurologist in the clinic (9.5%). Twelve percent of the respondents have mentioned doubts about qualifications of the medical professional as a reason to not go to the clinic. Ten percent of the participating patients are not motivated enough to seek outpatient care, and

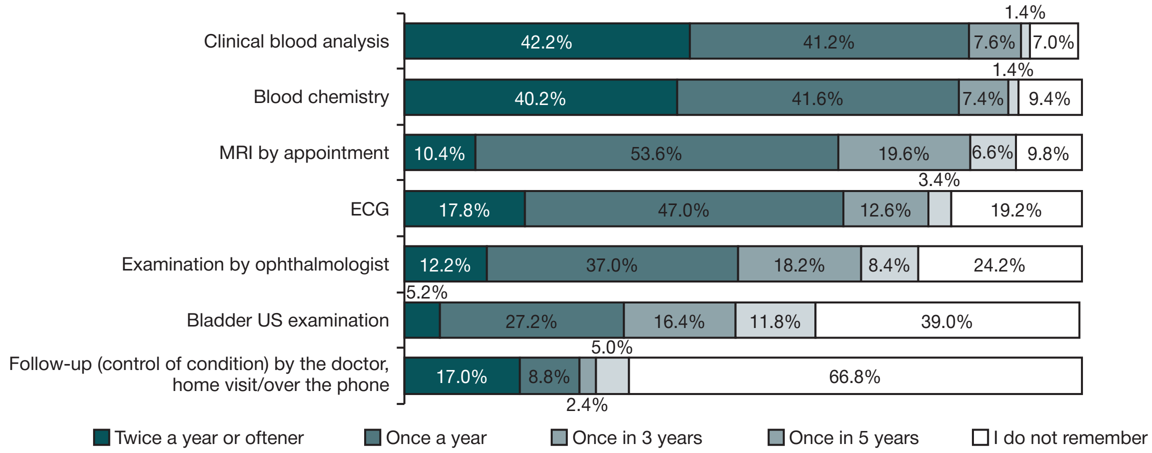

Diagram 6. Frequency of examinations

6.2% are too busy to to go the clinic. Diagram 6 shows the frequency of instrumental examinations underwent by patients with SPMS. (Diagram 6.)

The proportion of SPMS patients receiving care at home is 12.6% of the total number of respondents. Forty-one percent of the study participants have voiced unfulfilled need for such care, i. e., home medical assistance is unavailable to them. This is a significant share of SPMS patients who have difficulties with visiting the clinic and need patronage. The medical professionals that typically pay visits to SPMS patients are physicians (11.2% of the respondents) and neurologists (7.6%); the frequency of such home visits is once or twice a year. In individual cases, the patients are visited by a registered nurse, a massage therapist or an exercise therapy professional.

Treatment in regional MS centers and specialized departments of hospitals. In addition to outpatient medical care, patients with SPMS, as necessary, undergo treatment and rehabilitation in hospitals.

Currently, MS centers offer basic types of rehabilitation: exercise therapy, physiotherapy, massage (according to 80–87% of the neurologists interviewed). As stated by 74.4% of the participating medical professionals, patient organizations participate in the work of most MS centers. Sixty-two percent of neurologists highlighted the possibility of provision of psychological assistance at the MS centers. As for trips to health resorts, 41% of the respondents said that far from all MS centers offer them. According to the survey, 89.2% of patients diagnosed with SPMS are observed in specialized MS centers. A fifth of the participating patients (20.8%) are admitted to MS centers for inpatient care once a year, while 22% stay in the hospitals once every 2–3 years and 31% — less than once every three years. There are also patients that undergo inpatient treatment and rehabilitation in MS centers more often than once a year (12.2% of the respondents). SPMS patients take rehabilitation courses in an outpatient setting very rarely: over 75% of the respondents stated they have never done so.

In addition to treatment at the regional MS centers, MS patients are occasionally admitted to the neurological departments of hospitals. According to the survey, less than half of patients with SPMS received such inpatient treatment outside MS centers (43.8% of the respondents). In most cases (73.2%), the stay at the neurological department of a hospitals lasts up to two weeks.

The most common reasons for admission to a hospital are exacerbation of the disease (40% of the respondents) and its general aggravation (37%). Among other reasons, in isolated cases, the respondents mentioned the need to refine therapy, clarify the diagnosis or remedy the side effects of a previous therapy; 17.8% of the patients admitted to a hospital could not state the reason for admission clearly. Diagram 7 shows the reasons why 230 patients rarely seek inpatient care. (Diagram 7)

Specifics of drug therapy for SPMS. Evaluation of the drug component of therapy is the most important aspect in the analysis of quality of medical and social care. According to medical professionals, currently, regional MS centers offer courses of symptomatic, pathogenetic immunomodulatory or immunosuppressive therapies, and vascular-metabolic therapy. Seeking to analyze the role of drugs in SPMS therapy, we asked the participating patients to name the drugs that they are taking currently and have been taking before, and to indicate the duration of their intake and methods of obtaining them. The answers allowed making the following observations regarding the specifics of drug therapy for SPMS. Today, SPMS patients tend to take drugs from the following groups: Interferon beta-1b — 33% of patients, Interferon beta-1a — 14.6% of the respondents, Natalizumab — 10%, Glatimera acetate — 9.5%, Teriflunomide — 8.5%. Drugs that SPMS patients have been taking before: Interferon beta-1b — 73.3% of the respondents, Glatiramer acetate — 45.3%, Methylprednisolone and other glucocorticosteroids — 30.7%, Interferon beta-1a — 28%, Mitoxantrone — 14.4% of the participating patients. The vast majority of patients receive drugs free of charge. In isolated cases, patients independently purchased Interferon beta-1a s. c., Alemtuzumab, Methylprednisolone, Ocrelizumab.

The most common active agents in doctors' prescriptions are: interferon beta-1b, interferon beta-1a, methylprednisolone, ocrelizumab, mitoxantrone.

As for the interviewed medical professionals, currently they prescribe the following drugs to patients with an established diagnosis of SPMS: Interferon beta-1b (90.2% of the respondents), Methylprednisolone and other glucocorticosteroids (60.8%), Interferon beta-1a (43.1%), Ocrelizumab (41, 2%), Mitoxantrone (39.2%), Natalizumab (25.5%), Teriflunomide (19.6%), Alemtuzumab (19.6%), Glatiramer acetate, fingolimod and pegylated interferon (17.6% each name), Dimethyl fumarate (9.8%). (Diagram 8)

Throughout the length of their practice, the participating doctors have been prescribing: Interferon beta-1b (84.4% of respondents), Methylprednisolone and other glucocorticosteroids (77.8%), Mitoxantrone (62.2%), Interferon beta-1a (57.8%), Glatiramer acetate and pegylated interferon (37.8% each), Natalizumab (33.3%), Fingolimod (31%), Teriflunomide (26.7%), Alemtuzumab (22.2%), Dimethyl fumarate (17, 8% of respondents). The primary guides for doctors in prescribing drugs to SPMS patients are the clinical

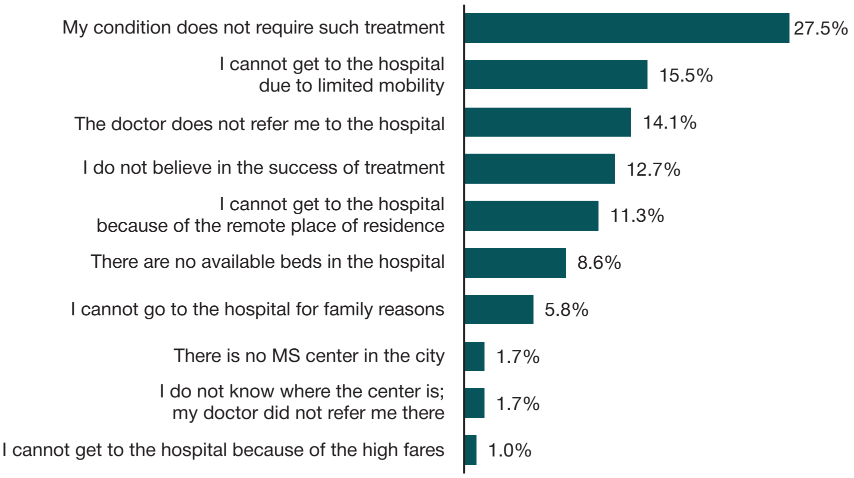

Diagram 7. Reasons for refusal to undergo hospital treatment, % of those who answered the question

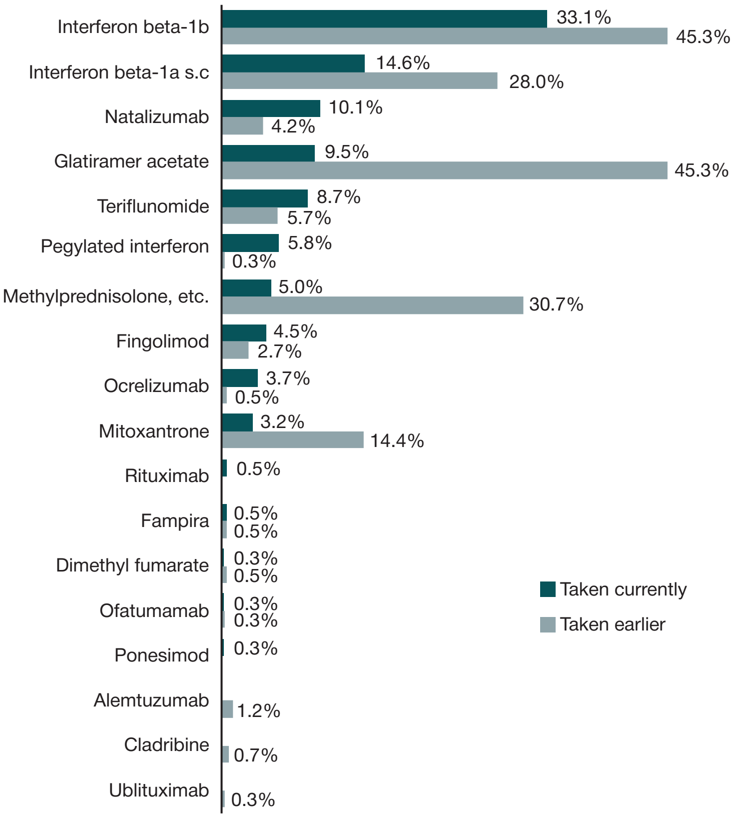

Diagram 8. Drugs taken by SPMS patients at different times

picture and the specifics of the course of the disease, as well as the existing standards and recommendations of the specialized federal government body. (Diagram 9)

Interviewed neurologists mentioned that, selecting drugs to prescribe, they perform a comprehensive assessment of the patient's condition, factor in comorbidities, patient's psychophysiological condition, including the degree of his/her cognitive and emotional impairments. A dynamic assessment of the patient's condition based on examination supports the doctor's opinion about the need to change the treatment regimen and prescribe drugs. The responses given by the participating medical professionals indicate that they monitor patient's condition based on the laboratory blood tests and MRI data. Dynamic observation allows evaluating the efficacy of the previously followed therapy in order to select the most appropriate treatment regimens while factoring in individual reactions of the patient.

The success of therapy largely depends on the motivation of patients, their adherence to therapy, awareness of the desired result and willingness to follow doctor's recommendations. When the patient feels comfortable in treatment, the chances of his/her adherence to the therapy throughout go up, which is why medical professionals, when prescribing drugs, also pay attention to the convenience of using them (how easy it is to dilute them, dose and administer).

The duration drug therapy courses varies. Glatiramer acetate and interferon beta 1-b are often taken for a long time: 52.6% of the respondents said they have been taking glatiramer acetate for over 4 years, and 36.2% of the patients stated the same about interferon beta 1-b. The estimations given by doctors and patients in this connection are quite similar. As for interferon beta 1-a, the duration of its intake is different: from several months (26.9%) to more than 4 years (22.7%). Teriflunomide and

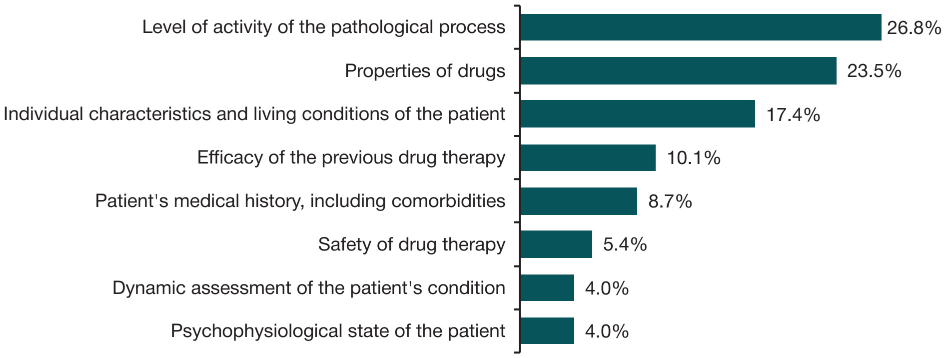

Diagram 9. Criteria of selection of therapy for SPMS patients (answers from neurologists)

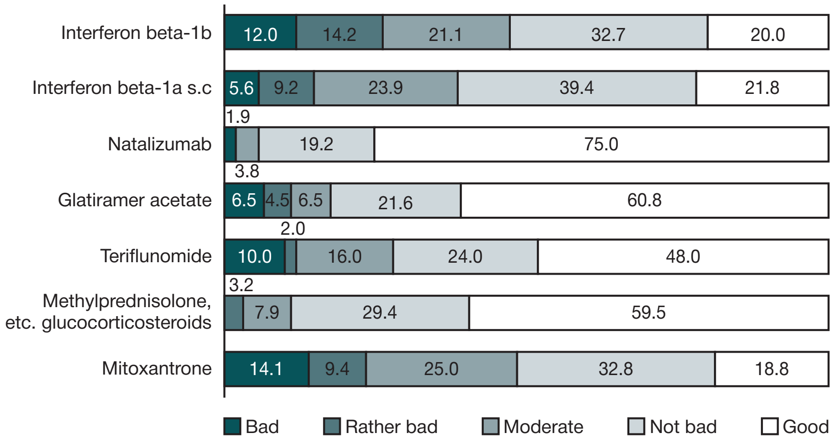

Diagram 10. Tolerability of drugs by patients with SPMS, in % for each drug

Natalizumab are taken for a relatively short period, only up to 2 years (97% and 69% of the participating patients, respectively). Pegylated interferon is also among the drugs that are taken mainly for up to a year (13 patients out of 15 mentioning this drug). Fingolimod was noted by 75% of respondents as a drug they have been taking for up to 3 years. Diagram 10 shows the tolerability of drugs by SPMS patients. (Diagram 10)

Evaluation of the efficacy of SPMS therapy. Patient satisfaction with the medical care they receive is a relative subjective indicator of its efficacy, which, nevertheless, can influence the further course of the disease, determining the quality of life with a chronic condition. The opinions of SPMS patients about the efficacy of drugs they take differ. Almost half of the respondents (48%) believe that drugs help. Sixteen percent of the respondents report no effect from drugs. Another 28% of the study participants rated the efficacy of drugs they take neutrally.

Patients' opinions of the effectiveness of treatment and rehabilitation in MS centers are mostly positive: the share of positive assessments is 2.5 times higher than that of negative assessments (47.4% versus 17.6%). According to the surveys conducted by the All-Russian Public Organization of Disabled People with Multiple Sclerosis, the dissatisfaction of patients with therapy is often associated with accumulated fatigue from the manifestations of the disease and disbelief in the success of subsequent manipulations.

Neurologists have differing opinions about the quality of medical care for patients with SPMS. Less than 15% of them are of very low opinion, while 24% believe the quality of care is “mediocre”. Sixty-two percent of the interviewed medical professionals believe the level of care provided to SPMS patients is above average. The majority of interviewed neurologists (68%) believe that the quality of medical assistance to MS patients is better in their region than generally in the country. It should be noted here that such appraisals may be attributed to the fact that many of the neurologists that participated in the study are practicing in large MS centers in Moscow, St. Petersburg, Samara and Kazan.

The overall opinion of MS DMDs therapy for SPMS expressed by the participating neurologists cannot be called high. Negative appraisals significantly outweigh positive ones: only 12% of the interviewed medical professionals had a positive opinion about pharmacotherapy received by patients with SPMS. The vast majority of doctors — 76% — consider it insufficiently effective, and 12% believe it is completely ineffective. Neurologists also think that the problem of provision of MS centers with effective drugs is quite acute. Seventy-five percent of the doctors surveyed indicated a high need for effective drugs for SPMS seen at such centers. Despite the high demand for effective drugs, medical professionals also point out the potential problems that may arise as effective SPMS therapy becomes available. The first problem is legal registration of the new drugs. Doctors (83.7% of the respondents) believe that if the new drug is not part of the federal list of “14 nosologies”, its registration will be a complicated matter. Other reasons for concern are the facts that the new drugs are not mentioned in the list of Vital and Essential Drugs (opinion shared by 53% of the respondents) and in federal clinical guidelines (45% of the respondents). There is another aspect that makes provision of drugs a complicated matter in the context of change of prescriptions: 43% of the participating doctors point to difficulties associated with diagnosis revision from latent RRMS to SPMS, and 22.4% mention complications arising in the process of identifying the patients that need therapy. According to the doctors, the main problems with treating patients in MS centers arise from the lack of effective drug therapy and clinical SPMS management guidelines.

Appraising the efficacy of rehabilitation measures, medical professionals believed the best options were psychological assistance, assistance from a patient organization and exercise therapy. Treatment at health resorts, massage, and physiotherapy scored lower. Answering an open question about the problems in organizing rehabilitation for SPMS patients, neurologists revealed different aspects:

1. Lack of a full-fledged rehabilitation system and its regulatory framework, which is a basic general problem from which many particular ones follow. There are no rehabilitation programs, rehabilitation rooms and departments, day care departments, health resorts offering relevant treatment. The doctors interviewed pointed to the fact that rehabilitation is not in the list of services covered by the compulsory medical insurance, and it is difficult to book a course through a doctor. Rehabilitation as activity is in the scope of the Ministry of Social Protection, which puts it out of competence of RS centers. Moreover, there are no codes and regulations governing establishment of rehabilitation centers offering a complex of medical and social services. There are also no regulatory documents on the standards of rehabilitation and patient referral. Treatment standards for MS do not provide for rehabilitation measures. In reality, the rehabilitation of MS patients often takes form of arresting exacerbations in MS centers.
2. Physical inaccessibility of MS centers for people with restricted mobility is the second most pressing problem voiced by neurologists. Such centers typically operate in regional capitals, and frequent regular visits (once every three months) thereto is a difficult task for people living in remote areas. Today, there is no established procedure facilitating trips to an MS center, it is not possible to bring the patients there. There are no mobile teams at the centers nor outreach services that would perform diagnosing and basic rehabilitation activities at home. Currently, outpatient rehabilitation activities are non-existent. In remote areas, there are no rehabilitation opportunity available in any form.
3. Lack of effective drugs designed specifically for treatment of SPMS is the third most frequently mentioned problem. In this connection, the respondents spoke about the “14 nosologies” list and that there are no SPMS-specific MS DMDs there with proven efficacy. The lack of effective therapy designed specifically for SPMS, according to the medical professionals interviewed, raises concerns of both neurologists and their patients, who stop visiting the doctor when RRMS transforms into SPMS because they know their current therapy can be canceled, which is what they are afraid of.
4. Administrative problems in the work of MS centers stem, as mentioned by the doctors, from the lack of a regulatory framework governing their operations. In a number of regions, such centers exist as departments of hospitals, and in some cases, there are either no or too few job positions under them, which translates into overloaded neurologists who work part-time and are often driven by their enthusiasm exclusively. Another manifestation of this problem is the limited number of beds and low capacity of MS centers, which complicates admittance for the patients.
5. There is a problem that is common for all MS centers: the rehabilitation programs offered there are too focused, and there are no clinical guidelines covering rehabilitation of patients with MS and SPMS. According to the doctors working at such centers, today they do not have a license for rehabilitation activities. The interviewed professionals mentioned lack of facilities for neurorehabilitation, general unavailability of equipment for rehabilitation of neurological patients, mechanotherapy, yoga therapy, aquatic procedures, psychological assistance. SPMS as a condition imposes its own limitations on the possibilities of rehabilitation. In some centers, exercise therapy physicians refuse to work with SPMS patients because they are convinced such patients have no rehabilitation potential.
6. Insufficiency of the physical infrastructure (materials and equipment) of RS centers. Addressing this issue, the respondents spoke about lack of necessary equipment, both medical and common, including specialized beds and bathroom aids. Auxiliary care products and mobility aids were mentioned as available in insufficient quantities.
7. Lack of a clearly defined SPMS treatment algorithm: a single diagnostic algorithm, clear clinical guidelines for patients with SPMS.
8. Problems encountered by SPMS patients in the clinics: first line neurologists know little about MS (and SPMS in particular) and side effects of MS DMDs, MS patients do not receive proper attention from the staff and have to make two “stops” before they get an appointment with an MS center neurologist (physician — neurologist of the clinic — neurologist of the MS center).

Measures needed to improve the quality of therapy and rehabilitation of SPMS patients, according to medical professionals. The interviewed neurologists state that in order to solve the problems existing in the system of rehabilitation of patients with SPMS it is necessary to update regulatory documents governing rehabilitation of patients (71.7% of the respondents), purchase new rehabilitation technologies (61%), adopt better patient referral patterns (39%), train staff (24% and 32.6%), optimize the approach to registration of SPMS patients (24%). As for the quality of medical care offered to patients with SPMS its improvement calls for additional trainings for clinic neurologists, cooperation between regional healthcare systems and regional MS patient organizations, involvement of federal centers in the differential diagnosis procedures, budget-supported MRI examination of the spinal cord in debatable cases, organization of work with relatives of patients.

In general, neurologists see the optimization of the system of medical care for MS patients reflected in the following steps:

- Update of the regulatory documents governing rehabilitation of MS patients.
- Development of regional programs designed to help people with MS.
- Expansion of the list of drugs for MS: inclusion of new effective drugs in the federal list of “14 nosologies”, federal clinical guidelines and the list of Vital and Essential Drugs.
- Improvement of the patterns of prescription of MS DMDs in SPMS cases.
- Establishment of specialized MS centers where they currently do not exist.
- Improvement of the physical infrastructure (materials and equipment) of the MS centers.
- Procurement of the new rehabilitation technologies.
- Training staff for RS centers to cover the current shortage.
- Advanced training of neurologists working at outpatient clinics to have them detect the disease at earlier stages.
- Introduction of the proper MS patient referral patterns.

CONCLUSION

The study revealed a significant variability in the social status and living conditions of patients with SPMS. According to the authors, the problems associated with provision of medical care to this group of patients are vivid to the medical professionals surveyed. The measures proposed by the doctors to eliminate the problems of providing medical care to patients with SPMS are, in the opinion of the authors, relevant and appropriate, and their list is quite complete. The authors believe that the matter of registration of highly effective drugs for SPMS in the Russian Federation is one of the most important steps. At the same time, the results of this study suggest the high significance of the patients' own motivation and adherence to therapy. These parameters directly depend on how clear and convincing the arguments in favor of the treatment sound for the patient, how convenient the MS DMDs are to use and how comfortable the therapy is in general.

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