Evaluating Treatment Decision for Multiple Sclerosis: Real Life and Patient Experiences

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ABSTRACT

There are different decision-making models in medicine for treatment decisions. Shared decision-making model is the most appropriate and widely used model for chronic diseases like Multiple Sclerosis (MS). In this model, the decision making process like treatment options is being discussed step by step between patients and physicians. However, increasing treatment options and medication side effects make the

decision-making process more difficult for physicians and reveal the need to share wider knowledge with the patient. In this article we evaluate treatment decision making in patients with MS involving real life experiences.

Keywords: Multiple sclerosis, shared decision making model, treatment decisions

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MAKING TREATMENT DECISIONS IN MULTIPLE SCLEROSIS

It is required to make decisions at several stages in MS for treatment decisions. First the physician must decide whether there is a need for using immunomodulating drugs (IMD) or not. Clinical characteristics and magnetic resonance imaging (MRI) properties of the patient should be considered and discussed during the decision making process first amongst the care giving medical team and then with the patient. Once starting a treatment is decided the question of which IMD to use awaits in the second stage. It is necessary to monitor the effectiveness of treatment with clinical follow-ups and MRI periodically after the initiation of treatment. During the process, sometimes the need for changing the current IMD or ending the treatment may emerge because of different reasons like pregnancy or disability progression. There are two sides in the decision making process: The Patient and the physician. Easily accessed but generally misinformative sources of information (social media, internet, newspapers, general information about illness and drugs from the booklets or fragments of information heard from other patients), the socio-economic status level of education and cognitive status of the patient may influence the decision-making process for the patient. On the other hand experience and knowledge are very important in terms of physician (1,2,3)

DECISION MAKING MODELS IN MEDICINE

Various decision-making models are available in the doctor-patient relationship (1). Physician makes the decision in a model and the patient is completely passive to decide or in an opposite model patient makes the treatment decisions. But more often shared decision-making model is used where patients and physicians engage in the decision making process equally. Sometimes the family is also involved in this process like family-controlled models (1).

Patient is passive and dependent in the *paternalistic model* (2). Physician is the single decision-maker and patient participation is very limited. In this model the main task of the patients is taking the medicine given by the physician. This model is still widely used, especially in emergency room settings. "The doctor knows best" forms the basis of the paternalistic model. This model has long been criticized for being particularly intense in terms of patients' rights and medical ethics. However, in a disease like MS that requires long-term treatment it is very unlikely to have positive outcomes without taking the patient's decision into consideration during the treatment process. Patients need to participate in the treatment process due to the possible side effects or partial clinical responses to allow better cooperation (2).

Family relatives of the patients and their families participate in the decision making process instead of the patient in the *patient-centered model* (3). This model can be used depending on the type of the country's cultural characteristics. Participation of family members in the process of diagnosis and treatment can be useful in a disease like MS, which is a chronic, serious, heterogeneous disease with a prognostic uncertainty. Family members may be supportive in terms of treatment compliance (4).

Agent-based simulation model is another method for decision making in MS (3). In this model, the patient is informed in detail about treatment options like a pro. Patient give the treatment decision but physician is still router during the process (4).

Patients remain active and autonomous in *informative model* (2). Doctors do not participate directly in the patient's decision-making. However, the clinician is obliged to provide the information the patient needs to make a decision. The information given like medication effectiveness, side effects, and complications directly influences the patient's decision.

The *shared decision making model* is the most used in common practice. It is not only the model of treatment options spoken, it is also a two-way exchange of information between patient and physician (4). The basic features of this model are:

- Two participants (patient and physician) attend the treatment decisions.
- Treatment options are discussed step by step in the process of deciding on treatment.
- Patient and physician both offer their opinions on treatment.
- Patient and physician are in a consensus on treatment.

This model is widely used by many clinicians. The implementation of this model would be beneficial for making treatment decisions for MS. The main challenge in this model is; increasing treatment options, applying different conditions to these treatment options, risks and benefit rates, adverse events and complications complicate the decision-making process (4).

All possible treatment options for the patient's treatment should be offered to patients in the shared decision-making model. The most appropriate treatment option should be highlighted according to the patient's clinical situation, the social and cultural characteristics. Benefits and potential risks should be described to patient as openly as possible for appropriate treatment options (5,6). Physician should give descriptive answers to questions about the patient's treatment options. Physician must specify treatment options preferences and share information with the patient about risk and benefit for the treatment. At the final stage clinician must share his treatment choice with the patient using the evidence-based data and the patient's preferences. The choice of treatment should be administered by a joint decision of the patient and physician (7,8). Recently new therapeutic options have become available for the treatment of MS and more will be licensed in the near future. Although more efficacious and easier to administer, the new drugs pose increased risks of severe side effects (9,10). Facing increasingly complex decisions, patients need up-to-date evidence-based information and decision support systems in order to make informed decision together with physicians based on their autonomy preferences (6).

Patient's preferences, choices, cooperation, partnership, patient participation, patient-related concepts such as patient education have come to forward in the shared decision-making model (7). Patient is on one side of the treatment decision, the physician may be on the other side of it. The severity of illness, duration of illness, side effects, the number of treatment options, the patient's comprehension-level of perception,

experience of the physician, the physician's choice of treatment are all effective in decision making. At last, doctor and patient reach a shared decision (8).

IMPLEMENTATION OF SHARED DECISION-MAKING MODEL IN MULTIPLE SCLEROSIS

Patients and health authorities increasingly claim active roles in health care decision making processes. As immune therapies in MS are partially effective MS is a prototypic condition for a shared decision-making process. The treatment of acute relapses and the initiation, change or withdrawal of so called disease-modifying treatments are key decisions in MS management. The more the patient gets information about the disease the more their participation in treatment decisions increase. We need to use some materials to contribute patient education. Patient brochures, especially visually simple training materials are quite effective in this regard. Patient schools, long-term patient education programs may be useful for the patient participation in treatment (7).

Training is not only to affect long-term immunomodulatory therapy it has been found to cause a significantly decrease in the number of relapses in the coming period (9). Patients are able to better interpret the actual relapses with patient education programs. A study was conducted in 2015, it was determined that the MS nurse has implemented a training program for patients for 4-hour training program and at the end of treatment patients make the treatment decision was with better compliance (10). For example, when we started a relapse treatment in a patient, especially an inexperienced patient, we need to give answers to some questions: What is the purpose of the treatment? Does treatment reduce the disability in the next short period of relapse? Does treatment prevent new relapses? Is there any effect of treatment on the course of the disease? What are other treatment options? What is the chance of the recovery? What is the side effects and risk of the treatment? (Table 1) (11).

Table 1. Questions need to be answered in the treatment of MS relapses

•	What is the purpose of the treatment?
•	Does treatment reduce the disability in the next short period of relapse?
•	Is there any effect of treatment on the course of the disease?
•	What are other treatment options?
•	What is the chance of the recovery?
•	What is the side effects and risk of the treatment?

Treatment may not be started immediately after the diagnosis. Treatment options can be decided with the patient after a certain time, giving the patient opportunity to think about treatment options, so the treatment can be postpone a few months (10).

Which IMD drug will be started and how long to be is used, the timing of drug changes if enough responses cannot received or patient presents a progressive course, which drug to shift, drug discontinuation be required if disability occurs, at many points in a long process from beginning to end we need to sit together and give a unanimous decision with the patient. The duration of the disease, type of prognostic indicators are affect treatment decisions. The clinical progression of patients, MRI lesion load, drug efficacy, side effects, patient compliance with the drug, the patient's socio-economic status, education level, occupation, or the desire to have children affects treatment process (Table 2).

Table 2. Considerations during treatment decision in MS	
•	MS Type and duration
•	Prognostic Features
•	Drug Efficacy
•	MRI lesion load
•	Security, Side Effects
•	Drug's administration form (subcutaneous, iv or oral)
•	Patient's socio-economic status, occupation

CLINICAL EXPERIENCE SHARING

Case 1

30-year-old female patient, single, accountant. She admitted to the clinic with complaints of double vision and dizziness for 2 weeks. Her neurological examination revealed double vision in the right perspective, dysmetria and dysidiadochokinesia in the left, ataxic gait, vibration loss in the lower extremity and Babinski positive in the left. History and examination findings suggest brain stem syndrome. She had a sensory relapse in the right arm lasts 1 week and spontaneously recovered one year ago. MRI revealed lesions in the cerebellum and cervical regions without contrast enhancement (Figure 1a, 1b). Her complaints completely go off after 7 days of high dose methylprednisolone therapy within a month. There are two options: 1) we will follow up the patient with MRIs. 2) Start IMD. It must have been starting IMD for this patient. Which treatment do we start? Low-dose interferon, high dose interferon, glatiramer acetate, fingolimod, teriflunomide, dimethyl fumarate or do

we recommend natalizumab? Judging by the patients, which drug do patients choose? If we do not give enough information to the patient about drugs, application form, frequency of application so the patient naturally always choose the easiest way. Even patients if it is appropriate they do not want to use any treatment. It is needed to draw a frame to the patient and should give adequate information. We must give the patient possible options and we should specify like: "These are the alternatives but I find this appropriate for you". We started an IMD to this patient, but she did not use it. Approximately 1 year later she had right weakness as a relapse and resolved after high dose methylprednisolone therapy. There are new lesions and some of them had gadolinium enhancement in the follow up MRI (Figure 2a, 2b). After the third relapse we offered IMD more vigorously. Now she is using an IMD after the third relapse.

Case 2

34-year-old woman, married, teacher. She had a painful blurred vision in the right eye and improved by high dose methylprednisolone therapy for five days in 2012. She had a sensory relapse, numbness in the left of his face, in February 2013. There was a widespread periventricular lesion on brain MRI (Figure 3). Glatiramer acetate treatment has started and shifted to interferon beta due to some side effects. She had not a relapse at the end the first year of interferon therapy. She had no children, she was considering pregnancy. We can suggest the patient to continue treatment because we can say interferons and glatiramer acetate has no serious toxicity to infants and may not to be stop even during pregnancy. When the pregnancy is detected these drugs can be stopped if she has not any additional gynecological or genetic problems. She

Figure 1. Demyelinating lesions in the right cerebellopontine junction and in the C2-3 cervical regions.

Figure 2. a, b. There is new lesion in the left, near the lateral ventricle-posterior horn (a). Post contrast series showing halo shaped gadolinium enhancement (b, white arrow).

Figure 3. Brain MRI revealed widespread periventricular lesions.

gave birth to a healthy child and consult with us in terms of postpartum lactation. Here it is reasonable to continue breast-feeding and should not be initiated immunomodulatory drugs. In the follow up MRI within the 9 months of breastfeeding, there is a new T2 lesion and a contrast enhancing lesion (Figure 4). The patient has no new relapse, no clinical activity, but there were two new onset active lesions on MRI. The patient wanted to continue to breastfeed child until the age of two. However, we recommend the patient should be started immunomodulatory drug and stop breastfeeding.

Case 3

36-year-old male patient under interferon beta therapy for 6 years without a relapse. He suggested: "I am tired of interferon injection, put me on pills". We can explain him in what circumstances should be oral therapy started and oral drugs may have much more different side effects than injectable agents.

We should try to keep her on interferon as he has been doing well in this drug. We should discuss with the patient the possible side effects of new drugs. Moreover, optimal clinical efficacy of new the drug will begin within 4- 6 months. After discussing these handicaps of drug switch, we should offer patient to switch on oral drug if patient still want to stop injection. After shared decision-making we put him to an oral drug based on his wish.

Case 4

23-year-old woman, single. She has been using natalizumab for 4 years. She was switched from interferon beta treatment as relapses continued. After starting natalizumab disease activity, disability, clinical and compliance continued extremely well. JVC (+), index was 2.2, there is no history of immunosuppressive drug and she wants continue to medication. Patient continued natalizumab for 2 more years with follow-up MRIs for 3 months intervals as well as close clinical vigilance. Even patient was eager to continue, we had to stop natalizumab because of the increased risk of progressive multifocal leukoencephalopathy (PML) in the 6 year of natalizumab therapy, she was switched to fingolimod.

CONCLUSIONS

Patients want to have enough information about their health condition and treatment options, but they want the physician take the responsibility for treatment decisions. Although we give a shared decision in the MS treatment, physicians guide the treatment. Because there is a wide difference in terms of knowledge and experience, the router of MS therapy is the physician who experienced in this field and the patient should be informed about the therapy. .

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Figure 4. a, b. There is a new lesion in the right near the lateral ventricle posterior horn (a). This lesion has a gadolinium enhancement (b, white arrow).

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