Relapsing-Relmitting Multiple Sclerosis Patients' Experience with Natalizumab

A Phenomenological Investigation

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*This phenomenological investigation was undertaken to gain a better understanding of multiple sclerosis (MS) patients' experience with natalizumab (Tysabri; Biogen Idec Inc, Cambridge, MA) treatment and its impact on their quality of life (QOL). Twenty MS patients who were receiving natalizumab treatment were recruited by the physicians, nurse practitioners, nurses, and social worker of the William C. Baird Multiple Sclerosis Center in Buffalo, New York, between March 2009 and November 2009. Patients were invited to participate if they had relapsing-relmitting MS, had received at least six treatments of natalizumab, and could articulate their experience. An interviewer obtained informed consent, gathered basic demographic information, and then tape-recorded the participants' accounts of their experience with natalizumab. The audio-recorded interviews were transcribed and de-identified before being submitted to the investigators for analysis. The Atlas.ti qualitative data analysis program (Scolari, Berlin, Germany) was used to manage the data. Patients found natalizumab easy to tolerate and effective; moreover, they described improvement in their QOL. Patients must weigh the benefits of control of their MS against the increased risk of developing progressive multifocal leukoencephalopathy with natalizumab treatment. Information from this study will be used to educate professionals involved in MS patient care as well as patients and families considering treatment with natalizumab. *Int J MS Care.* 2012;14:39–44.*

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system that results in demyelination and axonal degeneration. Symptoms related to the neuronal tissue damage may include visual loss, weakness, imbalance, change in sensation, movement disorders, bladder or bowel dysfunction, depression, and cognitive impairment. Before the introduction of disease-modifying therapies (DMTs) in the late 1990s, there were no effective therapeutic interventions to alter the course of this progressive illness. Today, there are several DMTs with a variety of benefits, including natalizumab (Tysabri; Biogen Idec Inc, Cambridge, MA). Although it is a rare occurrence,

patients receiving natalizumab are at increased risk of developing progressive multifocal leukoencephalopathy (PML), a severe and often fatal brain infection.

The burdens of MS and its treatment may have a dramatic impact on patients' quality of life (QOL), which is defined by the World Health Organization¹ as the individual's perception of his or her position in life in the context of the surrounding culture and value system and in relation to personal goals, expectations, standards, and concerns. Improved QOL among people with MS has been associated with exercise,² cognitive and emotional stabilization,³ and improvement in physical and emotional components of health, as described in the pivotal placebo-controlled trial of natalizumab.⁴ The current study provides insight into the reasons for improvement in QOL among MS patients being treated with natalizumab.

Previous studies have documented experiences of patients with relapsing-relmitting MS (RRMS) using phenomenological methodology to provide a foundation for patient and professional education.⁵⁻⁷ The pres-

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ent study systematically investigated the experiences of patients receiving natalizumab in order to gain an understanding of their experiences and the impact of the treatment on QOL. Results of this study will be used to educate health-care professionals and to provide an accurate foundation for patient education and counseling.

Methodology

Design

The qualitative method of phenomenology used in this study evolved from the 19th-century philosophy of Edmund Husserl, who struggled to understand the human experience in terms of the subjective “lived world.”⁸ This lived world of the study participants embodied their experiences and senses of reality. Martin Heidegger, a student of Husserl, further developed the method used in this study.⁹ This method is generally referred to as Heideggerian phenomenology.¹⁰

Data Analysis

Approval to conduct this study was granted by the University at Buffalo, SUNY, Social and Behavioral Sciences Institutional Review Board. A purposeful sample of patients was derived in two ways: first, the physicians and nurse practitioners of the William C. Baird Multiple Sclerosis Research Center mentioned the opportunity to participate in the study to MS patients who presented to the clinic for care. If the patient expressed interest, his or her name and telephone number were given to the interviewer. The interviewer contacted the patient to arrange a convenient time to complete the consent process and the interview. Some participants were recruited by the interviewer in the infusion center as they came for their natalizumab infusion. The interviewer (MK) is a medical social worker who is available to provide patients at the William C. Baird MS Research Center with support. She did not approach clients with whom she had an existing professional relationship. The interviewer did not participate in the data analysis. The transcriptionist de-identified the typed manuscripts before submitting them to the analyzing investigators.

Patients were asked by the interviewer to describe their MS experience, with a focus on their current treatment with natalizumab. The interviews were audio-recorded and transcribed with all personal identifying information deleted. The data were then loaded into the Atlas.ti qualitative data analysis software program (Scolari, Berlin, Germany). The investigators extracted significant statements from the transcribed interviews

and then analyzed them to a higher level of abstraction to formulate meanings. The investigators responsible for data analysis performed the analysis independently and cross-checked their results for credibility, auditability, and fittingness. Themes were then developed from the formulated meanings and grouped into theme clusters. The data were saturated by the end of the 20th interview, indicating that there was no further new information to be extracted from the experience under investigation. Finally, the theme clusters were integrated into an extensive description of the phenomena, which patients verified from the perspective of their own experience.¹¹

Sample

The sample population consisted of 20 RRMS patients receiving natalizumab. The patients were between the ages of 22 and 65 years, with a mean age of 42.75 years. Participants had been diagnosed with MS 4 to 24 years earlier, with a mean of 11.75 years. Eighteen of the 20 participants were married. All participants had received prior treatment with a US Food and Drug Administration (FDA)–approved DMT for MS. Eight of the 20 participants had been previously treated with one DMT, while 12 had been treated with two or more DMTs. Additionally, five of the participants had received off-label treatments for MS.

Themes

Detailed analysis of the data from 20 interviews revealed five major theme categories: QOL, switching to natalizumab, uncertainty/fear, avoidance, and social support. There is overlap among the themes, which is to be expected in the lived experience.

Quality of Life

Quality of life was a pervasive theme among the participants. Quality of life was defined by the patients in terms of their ability to live a “normal” life without interruption by MS symptoms. Most, but not all, participants experienced improvement in at least one symptom of MS while receiving natalizumab. The improvement enhanced their perceived QOL. For those who did not actually improve, the destructive disease process may have stabilized.

Participant 1: *Tysabri has allowed me to be in life again, not watching from the sidelines. It has allowed me to go back to work and make a difference.*

Participant 4: *My endurance is much better. My fine motor skills are better. My balance is better. Generally, I'm*

more like my old self. It hasn't taken all my problems away, but I think it just makes it a lot more manageable, and my quality of life is so much better.

Participant 6: *I don't feel worse. I feel I am stable, and that's a bonus to be stable. So it's great. I'm not fatigued anymore. I don't have weakness like I did. You don't even think about it [MS].*

Participant 7: *I want quality of life, not quantity. If I don't go on this drug I could end up in a wheelchair for 20 years. In the beginning when I was on [DMT] it was really tough when she was a baby cause of the fatigue. But now, since the fatigue is gone, and I have a lot to do for her for school and shopping and getting ready for school, and just activities, um, it's doable. I don't have to find somebody to do it for me because I am too tired. I can do everything I need to do.*

Participant 19: *It's being able to do what I want and when, and you know, I mean and that's just, I can go to work, I can take care of my family, and um, you know, that's just the quality of life.*

Participant 18: *It's [QOL] a lot better now, it's a lot better, because like with the [other DMT] it just added to all the, all the side effects you have all day, adding to what you already have to deal with, you know, just, I don't know, made it worse than it had to be. So, here there's no side effects. I can go home and do whatever.*

Participant 15: *I am very happy that it [natalizumab] is keeping me as healthy as I am, regular daily tasks like a regular person. I can . . . I can take care of myself and my family. I can work part-time. I can take care of the house and I can . . . I have a great quality of life being on this medicine.*

Switching to Natalizumab

The switching theme includes participants' experiences and thought processes leading up to the change in treatment to natalizumab. They discuss their reasons for switching medicines as well as their fears of the change. There is also hope involved in switching medicines in the form of better tolerability and efficacy as well as better QOL. For many, switching to natalizumab greatly improved their QOL, as is reflected in the previous theme.

Participant 1: *They started me on [DMT] and the IV steroids and then I continued to exacerbate so I went from [another DMT] and IV steroids to methotrexate and the steroids and then [back to the other DMT] and [and yet*

another DMT] and the IV steroids. I continued to break through, so we started on Tysabri.

Participant 2: *It was obviously hard for my husband. It was a pretty big decision for us to come to, and he was right along with me at all the doctor appointments, understanding what was happening, what was going on. We came to the decision together, even though he stressed that it's my body, and I'm the one who needs to make the final choice.*

Participant 5: *Oh, I cried. I was scared. But I trusted [provider]. That's what she felt that I needed to be on, I was going to do. I had to do something, I knew that. So I did it and I am glad I did it.*

Participant 7: *I didn't feel that it was going to be a big risk for me because I trust my doctors, and I don't think they really pushed it if they didn't feel confident in the drug.*

Participant 14: *[Another DMT] I hated because it was so painful.*

Participant 20: *On the [another DMT] you always had that lethargic feeling for like a day or two. With the [yet another DMT], I didn't like it because of the injection sites. I always felt like I was hurting in those spots.*

Uncertainty and Fear

Uncertainty and fear are inseparable concepts and are emotions experienced by all of the study participants in some form. Uncertainty is unavoidable in the MS experience and begins with the first symptoms and diagnosis.¹² Then there is the daily uncertainty as to whether the MS will bring a deterioration in function or is actively destroying the patient's nervous system. Patients are never quite certain that they have made the right treatment decisions after weighing the benefits and risks.¹³ Fear of the future rings through each of the participants' stories and appears to motivate them to consider stronger therapies with higher risks. Despite the fact that switching to natalizumab created new fears, several participants complained that the risks of natalizumab were overemphasized and that insufficient attention was given to the potential benefits.

Participant 1: *Before the Tysabri I was always breaking through on my medications, so I always had the fear of doing too much, you know, so I would stop myself maybe from doing things even when I thought that maybe I could. I was always afraid to push. So that fear of getting sick stopped me from doing a lot.*

Participant 2: *I'm sure anybody who goes on Tysabri from the moment they make that decision . . . worry about PML.*

Participant 5: *Every day I'm always grateful. I'm always afraid every day that it's going to end.*

Participant 5: *I cried. I said I can't be on Tysabri, I have kids. And she said that is exactly why I want you to be on Tysabri. . . . I was so afraid to try Tysabri, you know, the warnings and the labels are just, they're so scary. It's such an amazing medicine that I just wish it was advertised differently to people, that they knew the amazing things that it can do, and not made to sound like an awful drug. I understand that it is powerful, but it's powerful because it can do some pretty powerful things.*

Participant 15: *My husband had more fears than anything. He was worried about the brain infection.*

Avoidance

Participants mentioned avoidance frequently. Some used avoidance as a way of coping with fears of the disease. Instead of having to make decisions about treatments or undergo the unpleasantness of them, the patients simply avoided situations such as office visits and taking their medications. Some recalled that they switched to natalizumab because it would make it more difficult to avoid treatment than it was with other modalities. In the infusion suite, some participants tried to avoid facing the disabling consequences of MS by isolating themselves from others receiving infusions.

Participant 2: *I didn't want to go for MRIs every year. Who wants to think they are sick? So I stopped going for MRIs.*

Participant 13: *He sent me for an MRI, and they said I had scattered foci. So I kind of, you know, blew it off, like yeah, you know, whatever.*

Participant 16: *I don't want to know. I work in a nursing home and I see people with it in the nursing home. When I get my infusions I always sit in the end chair and usually I have my iPod on because they all talk about it [MS and its symptoms] . . . I don't like to think about it.*

Social Support

Participants acknowledged support in many forms and from a variety of sources. Family members were recognized as both positive and negative sources of support. Some family members could be obstructive to the diagnosis and treatment process. Most family members, however, were supportive and helped the patients cope

with the burdens of MS. Family members' fear of PML was pervasive. Ultimately, the patients receiving natalizumab noted that they needed less support when they were on natalizumab because they felt better. Health-care providers were perceived as part of the patient's support network, although not always in a positive sense, such as when the provider reported a worsening of the disease and the need to change to a more aggressive treatment. The importance of trust in the health-care team was emphasized.

Participant 1: *And my husband, we go out for dinner. We can laugh more. We can make plans. We do things, you know, and even in our relationship there is more energy, and you know, and that's all huge.*

Participant 2: *He [father] wasn't happy that I went on steroids. So needless to say, I was terrified to tell him about the Tysabri since he was really angry that I did the steroids. . . . I said I need to do this. I need to do something stronger. I kind of explained how I got it and he's been supportive ever since.*

Conclusion

Natalizumab is a treatment option for patients with relapsing forms of MS that offers benefits in controlling relapses and disease progression but is associated with an increased risk of the potentially fatal brain infection PML. The theme clusters of QOL, switching to natalizumab, uncertainty and fear, avoidance, and social support were synthesized into a description of the participants' experience with natalizumab.

Patients interviewed in this phenomenological study found natalizumab effective and easy to tolerate. They also described significant improvements in their QOL. Participants discussed their fears of worsening MS and the possibility of developing PML. This fear and uncertainty factor into the decision to change treatments. Once they started on natalizumab, their fears about the treatment abated, but the uncertainty about PML and the chance of worsening symptoms remained. Most participants found the natalizumab infusion experience to be very positive in a manner similar to a support group, but some found the infusion center atmosphere disturbing in that it forced them to encounter other MS patients with significant disabilities that they preferred not to think about.

By revealing the actual thoughts and experiences of MS patients receiving natalizumab, the results of this study will guide patient teaching about what to

expect with this treatment. We will also be better able to educate providers on how to overcome barriers and offer more effective support and monitoring. The fears and support barriers described by the patients in this sample provide a foundation for educating patients as well as their families. Future patients will be better able to balance their concerns about the treatment with the potential improvements in QOL that these participants describe.

Discussion

In a 2007 study, Rudick et al.⁴ documented improvement in both physical and mental measures of QOL in patients who received natalizumab that was not experienced by patients receiving placebo. The results of the present study support those findings and add insight as to possible reasons for the improvements in QOL. Even though many participants had fears or uncertainty regarding the risks associated with natalizumab, there was a pervasive emphasis on quality over quantity of life.

Previous studies have investigated patients' experiences with medications from a phenomenological perspective.^{6,7} The studies describe patients' experiences with interferon beta-1a (IFN β -1a) and with glatiramer acetate. Themes from the earlier studies were congruent with the themes of the present work. The experiences of the patients in the earlier studies (2001, 2006) focused more on side effects and issues surrounding frequent painful injections. This was not a strong focus in the present study, in which patients had fewer side effects and the actual administration of natalizumab was not an issue. Participants in the present study described enhanced well-being and QOL with natalizumab.

In all of the studies, one theme was related to choosing treatment, starting treatment, or switching to a new treatment. The specific considerations varied in deciding whether to select a particular treatment (IFN β -1a, glatiramer acetate, or natalizumab). All three studies reflected a concern with potential side effects. For those on IFN β -1a or glatiramer acetate, the concern was with immediate side effects after administration. In the present study, participants' concerns focused on the serious threat of PML.

Social support was a prominent theme in all three studies. Support was provided by family members and health-care providers. In all three studies positive support was sometimes lacking. The earlier studies revealed fears that were focused on injections and worsening of

the MS. In the present study, some family members were not supportive of the participant's switching to natalizumab because of anxiety regarding PML. Generally, however, family members were supportive and health-care providers were trusted.

Fear was more pervasive in the present study because of the deadly nature of PML. In the previous studies, fear was focused on injections and worsening of the disease.

Quality of life was emphasized in the patients receiving natalizumab. The efficacy and tolerability of available drugs for treatment of MS appear to be improving, although their associated risks may be greater.¹⁴ The risks of the newer medicines must be weighed against the detrimental effects of the disease itself on patients' QOL.

Limitations

Participants in this study were drawn from one MS center in Buffalo, New York, which limits the generalizability of the results. Patients from a different site may have an entirely different experience. The number of participants, however, was more than adequate for a phenomenological study.

All participants in the study demonstrated improvement while receiving natalizumab. It is unknown how their experiences may have differed from those of other patients receiving natalizumab who did not have similar results.

Implications

The results of this study provide insight into the educational and support needs of MS patients who are considering a switch in DMTs, as well as their families. The participants reported a disproportionate emphasis

PracticePoints

- Natalizumab can control MS disease activity, thereby dramatically improving patients' quality of life and in some cases "normalizing" their lives.
- The possible benefits of disease stabilization and improved quality of life offered by natalizumab must be weighed against the increased risk of progressive multifocal leukoencephalopathy, which is often fatal.
- The decision to take natalizumab affects the entire family; therefore, the family must be educated and supported in the decision-making process.

among health-care providers on the risks of the treatment, as opposed to the benefits and improvements to be derived. The positive and negative experiences reported during the infusion process can guide us to be aware of and attend to the privacy and support needs of patients. Finally, the fears and concerns of the families add to the participants' decision burden. MS care providers and support staff should take care to address the family's need to discuss their fears openly and to fully understand both the benefits and risks of the treatment.

Future Research

Duplicating this study with MS patients from a different MS center or even from a smaller practice may yield useful results and further capture the experience of this patient group. Studying patients who start on natalizumab and then stop treatment or demonstrate no improvement is also necessary. Future research on the specific themes of QOL, switching DMTs, fears, and so on will enhance our understanding of these patients' experiences and guide our nursing care. □

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