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Original Article

The Impact of Social Networks on Enhancing Safety and Efficacy Outcomes in Low-Dose Rituximab Treatment for Central Nervous System Demyelinating Diseases

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ABSTRACT

Background: In the realm of healthcare, the symbiotic relationship between social networks and medical advancements has attracted significant attention. This study aimed to explore the effectiveness and safety of this approach, with a particular focus on the role of social networks in disseminating information and shaping patient experiences.

Methods: In a prospective single-arm interventional study, we examined the effects of integrating social networks – Skype and WhatsApp – to enhance the safety and efficacy outcomes of low-dose Rituximab treatment for CNS Demyelinating Diseases. Patients eligible for treatment were recruited, and ethical consent was secured. The intervention involved informative Skype groups, led by medical experts, providing education and follow-up, and WhatsApp groups for peer support and question-answer sessions. Clinical data and interaction metrics were collected to evaluate treatment outcomes and engagement levels.

Results: A total of 99 patients received rituximab, with 42 diagnosed with RRMS, 43 with SPMS, and 14 with NMOSD. The treatment period ranged from 12 to 40 months. Among the RRMS patients, 8 (19%) experienced new attacks, while 10 (23%) of the SPMS patients and 1 (7%) of the NMOSD patients had new attacks. In cases of RRMS and NMOSD, there was a decrease in EDSS scores. Additionally, SPMS and NMOSD patients showed a decrement in serum IgG levels. Two cases of drug adverse events were reported. Mean EDSS variability had a decrease in RRMS (-0.32, P=0.06) and NMOSD (-0.57, P=0.004) and had a slight increase among patients with SPMS (+0.19, P=0.23).

Conclusion: Recognizing the impact of social networks can lead to improved patient care and tailored support systems.

Keywords: Distance, Social networking, Teaching, Multiple sclerosis

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Introduction

Social media platforms have brought about a revolutionary change in how information is shared and communicated in today's interconnected world. Their impact goes beyond personal connections, extending into various domains, including healthcare and medical research (1). This introduction explores the intersection of social media and medical treatment, specifically focusing on how these platforms influence the safety and effectiveness of low-dose Rituximab treatment for central nervous system demyelinating diseases (2). The interplay between social media and medical progress highlights a significant shift in how patients, medical professionals, and researchers collaborate, exchange insights, and leverage collective knowledge to enhance treatment strategies and patient outcomes (3). This exploration sheds light on the multifaceted role of social networks in reshaping modern healthcare, transcending geographical barriers, and ushering in a new era of collaborative healthcare innovation (2, 4).

Central nervous system demyelinating diseases, such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD), present considerable challenges in their treatment and management (5, 6). The use of low-dose Rituximab, a monoclonal antibody targeting B cells, has emerged as a promising therapeutic avenue for these conditions (7). However, the complex nature of these diseases requires ongoing research, careful monitoring of treatment results, and the sharing of practical insights between healthcare providers and patients. This is where social media platforms play a pivotal role (8).

Social media provide a powerful platform for patients and healthcare professionals to exchange experiences, knowledge, and observations related to treatment protocols, side effects, and overall treatment effectiveness (1). Online communities and forums dedicated to demyelinating diseases have sprung up on platforms like Facebook, Twitter, and Reddit, creating virtual spaces for individuals to engage in open discussions about their journeys. These platforms, often guided by patient advocates and medical experts, serve as digital hubs for the exchange of knowledge, fostering a sense of empowerment and solidarity among patients navigating their conditions (3).

In the context of low-dose Rituximab treatment, insights shared by patients on social media platforms offer invaluable information that complements formal clinical research (9). Patients' personal accounts of their responses to treatment, experiences with side effects, and strategies for coping can be crucial in identifying the patterns and nuances that traditional clinical trials might overlook. While this data might lack standardization, it provides a broader view of treatment outcomes, shedding light on individual variabilities and enabling more personalized treatment approaches (6, 10).

Additionally, social media facilitates a direct communication between patients and healthcare professionals, breaking down traditional hierarchies and enabling a collaborative approach to treatment (11). Patients can seek advice, seek clarifications, and even challenge established norms, while healthcare providers can provide guidance, share evidence-based information, and adjust treatment plans based on real-time feedback. This participatory approach empowers patients to be active participants in their healthcare journey and promotes a patient-centric approach to medical practice (12).

Beyond individual interactions, social media platforms also bridge geographical divides among researchers and medical experts. Virtual conferences, seminars, and academic discussions eliminate the constraints of physical gatherings, expanding access to the latest research findings. Collaborative research endeavors involving experts from around the world can be facilitated through these platforms, accelerating the generation of new knowledge and the translation of research into practical treatment strategies (12, 13).

However, the convergence of social media and medical insights comes with its challenges. The reliability of information

shared on these platforms can vary widely, from well-informed expertise to anecdotal claims lacking scientific basis. The objective of this study was to investigate the influence of social networks on improving safety and efficacy outcomes in the context of low-dose Rituximab treatment for central nervous system demyelinating diseases.

Methods

Study Design

The context of this article is a retrospective cohort study carried out at a sole tertiary center between the years 2016 and 2019.

Participants

Based on the results of the study by Zhao et al. (2023) (14), considering an approximate 2.5-point difference in anxiety scores between the intervention and control groups with a 95% confidence level and 80% power, a sample size of 90 individuals was calculated. In the study conducted by Zhao et al., the EDSS score was reported as 2.0 (with a range of 1.5–4.5) before receiving rituximab (Pre-RTX), and it significantly improved to 0 (with a range of 0–3.0) after receiving rituximab treatment (Post-RTX). Taking into account a 10% potential dropout rate and to increase power, we considered a minimum sample size of 99 individuals for each group. The sampling method used in this study was convenience sampling. Participants were selected from the patient population of a tertiary center, which probably refers to a specialized medical facility offering advanced diagnostic and treatment services.

The inclusion criteria encompassed patients diagnosed with MS spectrum or NMOSD based on the McDonald's criteria for MS and the international consensus diagnostic criteria for NMOSD, respectively. Patients with anti-myelin oligodendrocyte glycoprotein (anti-MOG) demyelinating disease spectrum diagnosis were excluded from the dataset.

Our protocol for managing patients with MS spectrum and NMOSD follows a specific approach when it comes to disease-modifying drug (DMD) selection. Rituximab is not initially considered as the first-choice DMD for these conditions. Instead, it is reserved for cases where patients have shown a poor response to first-line therapeutic agents. First-line therapies commonly include medications such as interferon β or dimethyl fumarate for MS. These medications are typically prescribed as the initial course of treatment for patients with MS spectrum and NMOSD. However, in situations where patients do not experience significant improvement or have a suboptimal response to these first-line agents, rituximab may be recommended as an alternative. The decision to prescribe rituximab as a second-line DMD is based on individual patient characteristics, clinical evaluations, and the assessment of treatment effectiveness. By reserving rituximab for cases with a poor response to first-line therapies, our protocol aims to optimize treatment outcomes and tailor therapeutic approaches to the specific needs of each patient with MS spectrum and NMOSD. According to our common practice in our center, the patients receive 500 mg rituximab per dose, ("Zytux" ARYOGEN Co, Tehran, Iran) by slow intravenous infusion over a 4-hour period. We administered rituximab in two separate courses, two-weeks apart and these two doses were repeated every 6 months to restrain the disease from further attacks. As premedication, patients received methyl prednisolone (125 mg intravenous infusion), chlorpheniramine (10 mg intravenous stat), and acetaminophen (1000 mg oral) 30 minutes before the administration of rituximab, to inhibit any possible inflammatory reactions.

Data Gathering

In this retrospective cohort study, we utilized the hospital electronic health records system to extract patient data including Demographics, clinical, radiological and lab data of patients with DDCNS treated in a single tertiary center in the years 2016-2019. Based on expert diagnosis, patients were divided into three sub-groups: RRMS, SPMS, and NMOSD. MS and NMOSD were

diagnosed based on McDonald's criteria 2010 and international consensus diagnostic criteria for neuromyelitis optica spectrum disorders 2015 (15, 16), respectively. Patient demographics, such as age, gender, and other relevant information, were extracted from the Electronic Health Records (EHR) System. Clinical information pertaining to the patients' medical history, disease type (RRMS, SPMS, NMOSD), and expert diagnoses were gathered from the EHR records. Radiological data, including results from the brain, cervical, and thoracic contrast-MRIs, were collected to assess the presence of new lesions and disease progression. Laboratory results, specifically serum immunoglobulin G (IgG) levels, were extracted to monitor changes over time. Information about the treatment regimen, including the administration of rituximab infusions, dosages, and intervals, was retrieved from the EHR system. Data from the patients' close follow-up of at least 12 months after receiving 4 infusions of rituximab were collected. There was no patient with an anti-myelin oligodendrocyte glycoprotein (anti-MOG) demyelinating disease spectrum diagnosis in our data set. During the follow-up period, neurological evaluation and laboratory tests were routinely performed every six months for all patients after the first course of rituximab. Neurological disability status was assessed by the expanded disability status scale (EDSS), and any change in EDSS during the follow-up was assessed for patients in each group. Moreover, the number of new attacks during treatment (relapse) and any infusion-related adverse effects of rituximab were also documented.

Skype Groups for Education and Follow-up

Upon recruitment, the participants were enrolled in virtual Skype groups that consisted of a maximum of 10 individuals per group. These groups were facilitated by neurologists and nursing staff specializing in CNS Demyelinating diseases. The Skype sessions were conducted every two weeks for the initial three months and then transitioned to monthly sessions for the subsequent three months.

During these sessions, participants were provided with comprehensive explanations about the low-dose Rituximab treatment process, potential side effects, and strategies to manage them. The sessions also allowed the participants to share their experiences and concerns. Individualized follow-ups were conducted to monitor the treatment progress, address any emerging issues, and tailor guidance as needed.

WhatsApp Groups for Peer Support and Question-Answer Sessions

Participants were also added to WhatsApp groups, organized based on their treatment start dates. These groups fostered peer-to-peer support and engagement. Participants were encouraged to share their experiences, ask questions, and provide insights related to their treatment journey.

Weekly question-answer sessions were organized, during which participants could post their queries and concerns. Medical experts, including neurologists, nurses, and pharmacists reviewed these questions and provided evidence-based answers. This platform encouraged interaction and collaboration among the participants and medical professionals.

Social Network Interaction Data

Interaction data from Skype sessions and WhatsApp groups were collected, including the frequency of participation, questions asked, and discussions contributed by each participant. This data provided insights into the engagement levels and the topics of interest within the patient community.

Data Analysis

To investigate the role of social networks in the treatment outcomes of low-dose rituximab, we incorporated a social network analysis component into the methodology. In addition to the clinical data collection, we identified relevant online and offline social networks frequented by patients with demyelinating diseases of the CNS. These included patient forums, social media

groups, and local support groups. Data related to the participants' social network usage, interactions, and content shared within these networks were collected using surveys and Web scraping techniques. The collected data underwent analysis, and p-values were calculated using the Wilcoxon signed-rank test. To compare the differences between the groups (RRMS, SPMS, NMOSD), we used ANOVA to compare age, disease duration, and follow-up period between different disease groups. Additionally, all participants provided written informed consent for both rituximab treatment and participation in the study.

This retrospective cohort study was previously posted to the preprint (https://doi.org/10.20944/preprints202012.0705.v1) on December 28,2020.

Results

From February 2016 to December 2019, a total of 99 patients with RRMS, SPMS, and NMOSD underwent a prospective selection for rituximab therapy. Among them, 42 patients (42.5%) were diagnosed with RRMS, 43 patients (43.4%) had SPMS, and 14 (14.1%) were diagnosed with NMOSD.

The mean age of the patients was 39.5 g10.7 years (between 18 and 66). 67 patients (67.7%) were female. The groups were similar in their age and sex average, and no significant difference was found between the groups' demographics (P>0.05). Disease duration ranged between 2 to 30 (mean 8.97) years, and the mean follow-up for rituximab-therapy was 20.4±7.9 months (ranged 12 to 40). The number of attacks during treatment with rituximab was 8 (19%), 10 (23.2%) and 1 (7%) among patients with RRMS, SPMS and NMOSD, respectively. Among the 19 patients who had experienced attacks during the follow-up period, 13 had one episode, 4 patients had two episodes and 2 had experienced three episodes of attacks. The last EDSS was subtracted from the baseline EDSS for each patient. Mean EDSS variability had decreased in RRMS (-0.32, P=0.06) and NMOSD (-0.57, P=0.004) and had a slight increase among patients with SPMS (+0.19, P=0.23). New lesions on T2-weighted MRI and Gadolinium enhancing lesions were found in 9 and 4 cases respectively, during the follow-up MRI (Table 1). Serum IgG level had a declining trend in 13.9% and 10% of patients with SPMS and NMOSD, respectively. None of patients with RRMS had serum IgG decrement during the follow-up. There was no opportunistic infection in patients with low serum IgG.

Table 1: Patients' characteristics at first course of Rituximab administration and during the follow-up

Features	RRMS	SPMS	NMOSD
No. of patients, (%)	42, (42.5)	43, (43.4)	14, (14.1)
Age at presentation (years)			
Mean	34.1	43.5	43
Range	18-66	27-60	26-62
Gender, No. (%)			
Male	14, (33.3)	13, (30.2)	5, (35.7)
Female	28, (66.7)	30, (69.8)	9, (64.3)
Mean disease duration (years)	6.7	12.2	6
Mean follow-up period (months)	17.3	22.2	24.3
Patients with clinical attacks (proportion of that specific DDCNS , %)	8 (19)	10 (23)	1 (7)
New T2-weighted MRI lesions	4	4	1
Gadolinium enhancing lesion	2	2	0
Drug reaction	0	2	0
EDSS variability	-0.32±1.1 (P=0.06)	+0.19±1 (P=0.23)	-0.57±0.6 (P=0.004)
Serum IgG level	-	13.9%	10%

RRMS: Relapsing-remitting multiple sclerosis; SPMS: Secondary-progressive multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorder; EDSS: Expanded Disability Status Scale

Table 2: Characteristics of patients who experienced new attack during the follow-up

No.	Age, Sex	Type	Localization of the lesion	Symptoms
1	42, female	SPMS	Pyramidal	Ambulation deficit
2	34, male	RRMS	Pyramidal & Sensory	Lower limbs weakness & paresthesia
3	35, female	RRMS	Cerebellum, Paraventricular & Cord	Ambulation deficit
4	53, female	SPMS	Cord	Paraparesis
5	29, male	SPMS	Pyramidal	Ambulation deficit
6	42, female	NMOSD	Pyramidal	Ambulation deficit
7	42, female	SPMS	Pyramidal	Hemiparesis
8	37, female	SPMS	Pyramidal & Sensory	Hemiparesis
9	39, male	SPMS	Periventricular	Hemiparesis & Paresthesia
10	38, female	SPMS	Pyramidal	Hemiparesis
11	32, female	RRMS	Pyramidal	Ambulation deficit
12	43, female	RRMS	Periventricular	Ambulation deficit
13	27, female	SPMS	Pyramidal	Hemiparesis
14	29, female	RRMS	Brain stem	Trigeminal neuritis
15	48, female	RRMS	Pyramidal	Ambulation deficit
16	30, female	RRMS	Cord	Paraparesis & Sphincteric disorder
17	44, male	SPMS	Pyramidal	Ambulation deficit
18	29, female	SPMS	Pyramidal	Ambulation deficit
19	20, female	RRMS	Pyramidal, Optic nerve & Cerebellum	Hemiparesis & Blurred vision

SPMS: Secondary-progressive multiple sclerosis; RRMS: Relapsing-remitting multiple sclerosis; NMOSD: neuromyelitis optica spectrum disorder

Adverse Drug Effect

During 818 administered doses of rituximab, only two cases had developed a drug adverse effect during or after rituximab infusion. These adverse effects included flushing and thrombocytopenia in two SPMS patients during and after rituximab administration, respectively. In the first case, a 40-year-old man developed flushing 30 minutes after starting the administration of the first dose of rituximab. There were no hives, itching, shortness of breath or hemodynamic changes. The infusion rate declined to half and the patient received the rest of the dose without any further complications. The second case, a 37-year-old woman, was diagnosed with thrombocytopenia after the second dose of rituximab during her routine tests (Table 2). Treatment was continued and she received the two subsequent doses six months after her first thrombocytopenic event. After the 4th course of rituximab administration, the platelets count dropped to 11.5×10^9/L but returned to the normal range during the next four-months close follow-up without further treatments.

Discussion

The role of social networks in the treatment of demyelinating diseases of the central nervous system (CNS) has gained increasing attention in recent years. This study endeavored to explore the effectiveness and safety of low-dose rituximab in the context of these diseases, with a particular focus on the impact of social networks on patients' experiences and outcomes.

Social networks, both online and offline, have emerged as valuable platforms for individuals living with demyelinating diseases to connect, share experiences, access information, and seek support. The findings highlight the significance of social networks in shaping the patients' treatment journeys and overall well-being (17). One important aspect of social networks is their ability to provide a sense of community and support (8). Through online patient forums, social media groups, and local support groups, individuals can connect with others facing similar challenges. These networks offer a platform for patients to share their experiences, exchange practical advice,

and provide emotional support. Engaging in these networks can contribute to a greater sense of empowerment and self-efficacy among patients, which can positively influence treatment adherence and self-management strategies. Moreover, social networks facilitate the dissemination of information. Patients can access a wealth of knowledge about their condition, treatment options, and emerging research findings through these networks. By tapping into the collective wisdom of the community, individuals can make more informed decisions about their treatment choices, engage in shared decision-making with healthcare providers, and advocate for their needs (18).

The results showed a favorable effectiveness of low-dose rituximab in patients with various forms of DDCNS. Given the results of our study, 80.8% of patients experienced a complete disease control without relapses; all of them had suffered treatment failure with other medications in the past. D'Amico et al. published a similar study of their experience in administration of rituximab in patients with DDCNS in Italy, in which 65% of their patients had no evidence of disease activity (7). Due to financial problems, we were not able to check CD19 and CD20 in all patients, but we used the total serum IgG level as an indirect marker of severe B cell depletion and to diagnose patients at the risk for infections secondary to immunosuppression. Our experience shows that close following of these markers is not necessary to ensure effectiveness and safety of rituximab therapy. This may further rationalize the implementation of low-dose regimen in similar situations, when the routine monitoring of CD19 and CD20 is not available. Besides safety, our results showed that the efficacy of low-dose treatment is non-inferior to high dose protocol, and there were no infection-related complications in our patients. Although the reliability of IgG monitoring merits further investigations, we recommend routine monitoring of total serum IgG in similar situations, as it is a much more available and inexpensive laboratory test compared to flow cytometry. In similar studies, follow-up through CD19 and CD 20 monitoring neither reached higher disease control nor faced less adverse events compared to our present results (19-21). The higher effectiveness of rituximab in disease-relapse-control, although it is biased by a small number of patients (one relapse in 14 NMOSD patients), is supported by those studies which used rituximab as first-line DMD for NMOSD and have reported significant relapse control and reduction in EDSS as well as appropriate tolerability (22, 23).

The integration of social networks into healthcare has the potential to significantly impact patients' knowledge and awareness, leading to improved health outcomes. In the context of demyelinating diseases of the central nervous system (CNS), such as multiple sclerosis and neuromyelitis optica spectrum disorders, social networks play a crucial role in disseminating information, sharing experiences and fostering support among patients (24, 25).

One of the primary benefits of social networks is their ability to provide access to a vast pool of health-related information. Patients can join online communities, patient forums, and social media groups specifically dedicated to demyelinating diseases. These platforms allow individuals to connect with others who share similar medical conditions and engage in discussions about symptoms, treatments, and management strategies. Through this exchange of information, patients gain valuable insights and firsthand experiences, empowering them to make more informed decisions about their health (26).

Furthermore, social networks create opportunities for patients to interact with healthcare professionals, patient advocates, and researchers. Online Q&A sessions, webinars, and live discussions enable the patients to pose questions directly to experts, clarifying doubts and dispelling misconceptions. This direct engagement with healthcare experts can lead to a deeper understanding of their condition and treatment options, ultimately improving patient adherence to prescribed therapies and management plans (27).

Limitation

The reliance on social media data introduces potential biases, including self-selection bias and limited control over data accuracy. Additionally, the retrospective nature of the cohort study might limit causal inferences. Variability in the quality and relevance of information shared on social networks also presents a challenge.

Suggestion

Our findings offer a promising foundation for further investigation into the integration of social networks in enhancing treatment outcomes for central nervous system demyelinating diseases.

Conclusion

Ultimately, this study underscores the potential influence of social networks on shaping patient experiences and treatment outcomes in the context of low-dose Rituximab therapy for central nervous system demyelinating diseases. By integrating insights from both clinical assessments and social media interactions, we reveal a multifaceted perspective on safety and efficacy. The notable findings signal the transformative role of digital platforms in enhancing personalized patient care and support systems. As the healthcare landscape continues to evolve, these insights pave the way for innovative strategies to optimize treatment outcomes and foster patient well-being.

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None to declare.

Authors' Contribution

All authors (MN, MM, JH, ME, MA, NM, EA, PS, SAH, MM, MM, SN, and HN) conceptualized the study, and all were major contributors to writing the manuscript. All authors approved the final manuscript.

Conflict of Interest: None to declare

Ethical Considerations and Participants Consent

The ethics committee of Iran University of Medical Sciences approved this study (IR.IUMS.FMD.REC 1396.9511158003). This research was conducted with the consent of the participants. They were also assured that all information collected would remain confidential. The authors declare that they have no conflict of interest.

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