Clinical Study

Quality of life in relapsing-remitting multiple sclerosis patients receiving CinnoVex compared with Avonex

Nahid Hatam¹, Peivand Bastani², Rahil Sadat Shahtaheri³

ABSTRACT

Objective: There is an increasing recognition among clinicians and researchers that the impact of chronic illnesses and their treatments must be assessed in terms of their quality of life (QoL) in addition to more traditional measures of clinical outcomes. The aim of this study was to compare the QoL in patients with relapsing-remitting multiple sclerosis (RRMS) using Avonex or CinnoVex.

Methods: We conducted a cross-sectional study on one hundred patients with RRMS, fifty and fifty patients were being treated with Avonex (Biogen Idec, USA) and CinnoVex (CinnaGen, Iran), respectively. We used a disease-specific questionnaire for MS (Multiple Sclerosis Quality of Life-54 [MSQoL-54]). Both groups were tested for significant differences regarding sociodemographic. A multiple linear regression model was constructed to find factors that affected the different aspect of QoL of the whole sample of patients.

Findings: MS groups did not differ in physical and mental health composite scores as well as relative scales. The results of regression models for each subscale showed that age, marriage, and Expanded Disability Status Scale were associated with several subscales of the MSQoL-54 (P < 0.05).

Conclusion: In this study, it was seen that there are no significant differences between QoL of Avonex and CinnoVex, but a limitation in our study the results may be different in other countries and even various areas in Iran.

Keywords: Interferon beta-1 alpha; multiple sclerosis; quality of life

INTRODUCTION

Multiple sclerosis (MS) is a chronic, neurodegenerative, inflammatory disease of the central nervous system.[1] Moreover, it is one of the most common causes of neurological disability in young and middle-aged adults.[2,3]

Three main types of MS are generally recognized: (i) relapsing-remitting MS (RRMS), (ii) secondary progressive MS, and (iii) primary progressive/remitting MS.[4] At disease onset, RRMS is diagnosed in approximately 80–85% of MS patients.[3,5]

Immunomodulation with interferon beta (IFN-β) is widely used to treat patients RRMS.[6] There is good evidence demonstrating the benefits of IFN-β in reducing relapse rates, slowing the progression of disability, and reducing MS disease activity.[7-9]

Intramuscular IFN-β1a (Avonex as a Biogen Idec, USA) is a member of the interferon family that is...
used to treat RRMS. CinnoVex is a biosimilar form of Avonex manufactured by CinnaGen Co., Iran.

This product has been approved for the treatment of RRMS by the Iranian Health Ministry.\[10,11\]

Quality studies including in vitro assays, impurity profiling, and clinical pharmacokinetic and pharmacodynamic studies were performed to demonstrate the physicochemical identical compound of CinnoVex to the original drug branded by Biogen Idec, Iran.\[12\] In addition, evidence from randomized clinical trials have shown that there are no significant differences between efficacy and side effects of Avonex and CinnoVex.\[10,12-14\]

Although the importance of quality of life (QoL) in clinical research has been extensively discussed over recent decades and there is an increasing recognition among clinicians and researchers that the impact of chronic illnesses and their treatments must be assessed in terms of their QoL in addition to more traditional measures of clinical outcomes such as morbidity and mortality.\[15‑18\]

No study has focused on comparing QoL for Avonex and CinnoVex so this study was conducted to compare the QoL of patients who used Avonex versus those applying CinnoVex.

**METHODS**

We conducted a cross-sectional study on one hundred patients with RRMS, while fifty patients were being treated with Avonex and fifty patients with CinnoVex. These patients had been registered in MS committee of the Special Diseases Department of the Shiraz University of Medical Sciences.

Inclusion criteria were (1) RRMS, (2) age: 18–70 years, inclusive, (3) using Avonex and CinnoVex for at least 12 months, and (5) Expanded Disability Status Scale (EDSS) ≤5.5. Following the selection procedure, the two groups were tested for significant differences regarding demographic and clinical variables. As seen in Table 1, the groups can be considered equivalent with no statistically significant differences between them ($P > 0.05$). All the patients signed the informed consent. The literate patients filled out the questionnaire by themselves. For illiterate patients, the questionnaire was filled out by verbal communication with unbiased test operators.

In all patients, clinical disability was measured by the EDSS.\[19\] QoL was assessed by Multiple Sclerosis Quality of Life-54 (MSQoL-54) instrument developed by Vickrey et al.\[20\] and validated in an Iranian population by Ghaem et al.\[18\] The scale consists of 54 items that are distributed in 12 multi-item scales and two single-item scales. The instrument includes questions from Short Form 36-item Health Survey as a generic core measure and 18 additional items specific for MS exploring health distress, sexual function, overall QoL, cognitive function, and energy. Physical and mental health composite scores are calculated as a weighted sum of selected domains to generate a simplified two-dimension solution to MSQoL-54 instrument. The subscales for the physical health composite summary are physical function, health perceptions, energy, role limitation-physical, bodily pain, social function, and health distress. The subscales for the mental health composite summary are overall QoL, emotional well-being, role limitation-emotional, cognitive function, and health distress. The composite scores range from 0 (poor health) to 100 (optimal health).\[21\]

Patients’ characteristics in both groups were compared using Pearson’s Chi-square for categorical variables and Student’s $t$-test for continuous variables. QoL scores were expressed as a mean ± standard deviation and qualitative variables as absolute numbers and percentages. Student’s $t$-test was used to assess differences between two groups for all continuous measures.

Finally, a multiple linear regression model was constructed by using summary scores of each dimension as dependent variables to find factors that affected the different aspect of QoL of the whole sample of patients, using patient groups as a constant factor. SPSS for Windows (Version 16.0. Chicago, SPSS Inc.) was used to analysis the data.

**RESULTS**

Results demonstrated that the differences in relation to demographic and clinical features were not significant between these groups [Table 1].

Table 2 shows the mean scores for 12 multi-item scales and two single-item scales and physical and mental health composite scores of the MSQoL-54 instrument. MS groups did not differ in physical and mental health composite scores as well as relative scales. As a result, there were no significant differences between both groups in health-related QoL (HR-QoL).

The results of multiple linear regression model that were performed to find factors that affected the QoL of the whole sample of patients using MSQoL-54’s scores as dependent variable are presented in Table 3. Our results after adjustment for age, sex, marital status, disease duration, and EDSS revealed that patient’s age was significantly associated with “physical function” and “overall QoL” subscales ($P < 0.05$).
Table 1: Characteristics of patients in Avonex and CinnoVex groups

| Indicator            | Avonex | CinnoVex | P   |
|----------------------|--------|----------|-----|
| Sex                  |        |          |     |
| Male                 | 10 (20)| 5 (10)   | 0.26|
| Female               | 40 (60)| 45 (90)  |     |
| Age group            |        |          | 0.67|
| 18-30                | 22 (44)| 15 (30)  |     |
| 31-40                | 14 (28)| 22 (44)  |     |
| 41-50                | 11 (22)| 9 (18)   |     |
| >50                  | 3 (6)  | 8 (4)    |     |
| Education            |        |          | 0.06|
| <12                  | 5 (10) | 14 (28)  |     |
| 12-14                | 11 (22)| 17 (34)  |     |
| >14                  | 34 (68)| 19 (38)  |     |
| Marital status       |        |          | 0.68|
| Single               | 18 (36)| 20 (40)  |     |
| Married              | 32 (64)| 30 (60)  |     |
| Disease duration (years) |      |          | 0.09|
| 1-10                 | 44 (88)| 40 (80)  |     |
| 11-20                | 6 (12) | 9 (18)   |     |
| >20                  | 0 (0)  | 1 (2)    |     |
| EDSS                 |        |          | 0.15|
| 0-2.5                | 36 (72)| 29 (58)  |     |
| 3-5.5                | 14 (28)| 21 (42)  |     |

P values refer to t-test or Pearson Chi-square. Data are presented as n (%). EDSS=Expanded Disability Status Scale

Table 2: Comparison of Multiple Sclerosis Quality of Life-54 scores between Avonex and CinnoVex groups

| MSQoL-54 measures      | Avonex      | CinnoVex     | P   |
|------------------------|-------------|--------------|-----|
| Physical health        | 64.57±16.73 | 62.65±17.87  | 0.57|
| composite score        |             |              |     |
| Mental health          | 63.26±19.83 | 61.99±19.38  | 0.85|
| composite score        |             |              |     |
| Physical function      | 72.3±24.7   | 71.1±23.1    | 0.8 |
| Health perceptions     | 61.7±21.8   | 62.3±21.12   | 0.89|
| Energy                 | 50.48±18.37 | 46.96±20.65  | 0.37|
| Role limitation-physical | 62.5±37.5  | 55.5±37.2    | 0.35|
| Bodily pain            | 71.06±20.17 | 69.3±25.45   | 0.701|
| Sexual function        | 73.96±25.2  | 63.61±29.8   | 0.14|
| Social function        | 76.8±20.99  | 74.17±18.15  | 0.504|
| Health distress        | 67.4±25.31  | 73.6±27.2    | 0.241|
| Overall quality of life| 69.6±20.65  | 66.4±19.6    | 0.43|
| Cognitive function     | 69.4±28.22  | 71.5±22.04   | 0.68|
| Emotional well-being   | 54.64±18.61 | 53.68±19.26  | 0.8 |
| Role limitation-emotional | 62.7±43.45 | 56±42.82     | 0.442|
| Satisfaction with sexual function | 63.28±26.92 | 61.66±29.16 | 0.821|
| Change in health       | 61±24.82    | 58.5±30.56   | 0.654|

P values refer to t-test between Avonex and CinnoVex groups. Data are presented as mean±SD. SD=Standard deviation, MSQoL-54=Multiple Sclerosis Quality of Life-54

As a result, worsening in physical and mental QoL health composite scores and their subscales were associated to higher age except for role limitation-emotional problems, but changes in age over the time did not impact significantly QoL measures except for physical function and overall QoL.

EDSS did not influence all QoL subscales, except for physical composite score (P < 0.05).

Sex and disease duration did not affect the QoL, whereas getting married was significantly related to a poor sexual function and overall QoL.

Moreover, marital status and EDSS were significantly correlated with “sexual function” and “overall QoL,” and “physical health” subscales, respectively (P < 0.05).

The specific HR-QoL scales model for physical health had the highest volume of variance explained (adjusted r² = 38%).

DISCUSSION

Results showed no significant differences between the studied groups in HR-QoL. Nafissi et al.[12] and Arababadi et al.[13] have shown that CinnoVex can be used as a safe and effective alternative to Avonex in the treatment of RRMS.

Moreover, Nafissi et al.,[12] Sharafaddinzadeh et al.,[14] and Etemadifar et al.[10] demonstrated that CinnoVex had the same effect on the reduction of relapse rate and EDSS progress as Avonex in RRMS patients and there is no significant differences between the Avonex and CinnoVex treated patients in case of experienced side-effects.

Jorgen et al.,[6] in a prospective study, found the associations between higher disability/older age at baseline and poorer HR-QoL at follow-up.

Simon et al.[21] reported that a higher age at inclusion was significantly related to a poor physical composite score as well as to physical function, role limitation-physical, bodily pain, and cognitive function. Changes in EDSS over the time did not impact significantly QoL measures. Disease duration did not affect the QoL, whereas a higher age at inclusion was significantly related to a poor physical composite score as well as to physical function, role limitation-physical, bodily pain, and cognitive function.

Pfaffengerber et al.,[22] in a single-center study demonstrated that EDSS contributed to both physical and mental HR-QoL and that age had an effect on the physical but not on the mental dimension.

To our knowledge, the present study is the first report on QoL of MS patients under two biosimilar forms of IFN-β1a: Avonex (Biogen Idec, USA) and CinnoVex (CinnaGen, Iran) treatment.
In this study, it was seen that there are no significant differences between QoL of Avonex and CinnoVex, but since this study was carried out in only one center, our sample may not be representative of whole patients with RRMS.

Prospective studies in a larger sample of RRMS patients are required to enhance the evidence of the drug impact on QoL. This study represents an opportunity to expand our knowledge on QoL of RRMS patients to pursue the ultimate goal of improving the QoL of patients who suffer from RRMS.[23] Furthermore, it seems that conducting other studies on the toxicity of these IFN-β products on this study population or the same patients may help to improve the knowledge along with presenting applied evidence for customized clinical guidelines in this area.

**AUTHORS’ CONTRIBUTION**

Prof. Nahid Hatam was designed the study and supervised it in all the methodological sections. Dr. Peivand Bastani was prepared the manuscript and technically edited the article, Miss. Shahtaheri was collected the data.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Bell C, Graham J, Earnshaw S, Oleen-Burkey M, Castelli-Haley J, Johnson K. Cost-effectiveness of four immunomodulatory therapies for relapsing-remitting multiple sclerosis: A Markov model based on long-term clinical data. J Manag Care Pharm 2007;13:245-61.

2. Weisshenker BG, Bass B, Rice GP, Noseworthy J, Carriere W, Baskerville J, et al. The natural history of multiple sclerosis: A geographically based study. I. Clinical course and disability. Brain 1989;112(Pt 1):133-46.

3. Weisshenker BG, Bass B, Rice GP, Noseworthy J, Carriere W, Baskerville J, et al. The natural history of multiple sclerosis: A geographically based study 2. Predictive value of the early clinical course. Brain 1989;112(Pt 6):1419-28.

4. Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis: Results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. Neurology 1996;46:907-11.

5. Richards RG, Sampson FC, Beard SM, Tappenden P. A review of the natural history and epidemiology of multiple sclerosis: Implications for resource allocation and health economic models. Health Technol Assess 2002;6:1-73.

6. Jongen PJ, Sindic C, Carton H, Zwanikken C, Lemmens W, Born G; Functional Composite and Quality of Life in Avonex-treated Relapsing Multiple Sclerosis Patients Study Group. Improvement of health-related quality of life in relapsing remitting multiple sclerosis patients after 2 years of treatment with intramuscular interferon-beta-1a. J Neurol 2010;257:584-9.

7. Panitch H, Goodin DS, Francis G, Chang P, Coyle PK, O’Connor P, et al. Randomized, comparative study of interferon beta-1a treatment regimens in MS: The EVIDENCE trial. Neurology 2002;59:1496-506.

8. Johnson KP, Brooks BR, Cohen JA, Ford CC, Goldstein J, Lisak RP, et al. Copolymer 1 reduces relapse rate and improves disability in relapsing remitting multiple sclerosis: Results of
a phase III multicenter, double-blind placebo-controlled trial. The Copolymer 1 Multiple Sclerosis Study Group. Neurology 1995;45:1268-76.

9. Kappos L, Traboulsee A, Constantinescu C, Erälinna JP, Forrestal F, Jongen P, et al. Long-term subcutaneous interferon beta-1a therapy in patients with relapsing-remitting MS. Neurology 2006;67:944-53.

10. Etemadifar M, Maghzi AH, Hoseinzadeh A. Comparing side effects of CinnoVex with Avonex in relapsing remitting multiple sclerosis patients. J Isfahan Med Sch 2009;27:93-100.

11. Etemadifar M, Mazdeh M, Torabi HR, Ghaffarpour M, Azimian M, Salami S, et al. A report of multiple sclerosis patients treated by CinnoVex™ in Iran. Tehran Univ Med J 2010;68:30-6.

12. Nafissi S, Azimi A, Amini-Harandi A, Salami S, Shahkarami MA, Heshmat R. Comparing efficacy and side effects of a weekly intramuscular biogeneric/biosimilar interferon beta-1a with Avonex in relapsing remitting multiple sclerosis: A double blind randomized clinical trial. Clin Neurol Neurosurg 2012;114:986-9.

13. Arababadi MK, Mosavi R, Khorramdelazad H, Yaghini N, Zarandi ER, Araste M, et al. Cytokine patterns after therapy with Avonex®, Rebif®, Betaferon® and CinnoVex™ in relapsing-remitting multiple sclerosis in Iranian patients. Biomark Med 2010;4:755-9.

14. Sharafaddinzadeh N, Majdinasab N, Ghiasian M, Moravej-Aleali A. Efficacy of interferon β1a (CinnoVex) in relapsing-remitting multiple sclerosis patients. Zahedan J Res Med Sci 2011;13:3-6.

15. Hahl J, Hämäläinen H, Sintonen H, Simell T, Arinen S, Simell O. Health-related quality of life in type 1 diabetes without or with symptoms of long-term complications. Qual Life Res 2002;11:427-36.

16. Ardito SQ, Bestetti RB, Cardinalli-Neto A, Otaviano AP, Nogueira PR. Chronic renal impairment in patients with Chagas cardiomypathy with chronic systolic heart failure: Prevalence and prognostic significance. Int J Cardiol 2011;152:133-4.

17. Joshi VD, Mooppil N, Lim JF. Validation of the kidney disease quality of life-short form: A cross-sectional study of a dialysis-targeted health measure in Singapore. BMC Nephrol 2010;11:36.

18. Ghaem H, Borhani Haghighi A, Jafari P, Nikseresht AR. Validity and reliability of the Persian version of the multiple sclerosis quality of life questionnaire. Neurol India 2007;55:369-75.

19. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). Neurology 1983;33:1444-52.

20. Vickrey BG, Hays RD, Harooni R, Myers LW, Ellison GW. A health-related quality of life measure for multiple sclerosis. Qual Life Res 1995;4:187-206.

21. Simone IL, Ceccarelli A, Tortorella C, Bellacosa A, Pellegrini F, Plasmati L, et al. Influence of interferon beta treatment on quality of life in multiple sclerosis patients. Health Qual Life Outcomes 2006;4:96.

22. Pfaffenberger N, Pfeiffer KP, Deibl M, Höfer S, Günther V, Ulmer H. Association of factors influencing health-related quality of life in MS. Acta Neurol Scand 2006;114:102-8.

23. Fisk JD, Brown MG, Sketris IS, Metz LM, Murray TJ, Stadnyk KJ. A comparison of health utility measures for the evaluation of multiple sclerosis treatments. J Neurol Neurosurg Psychiatry 2005;76:38-63.