Clinical Study

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

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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/relapsing 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

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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			0.26
Male	10 (20)	5 (10)	
Female	40 (80)	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 composite score	64.57±16.73	62.65±17.87	0.57
Mental health composite score	63.26±19.83	61.99±19.38	0.85
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. Values 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 $r^2 = 38\%$).

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.

Jongen *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.

Pfaffenberger *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.

Table 3: Multiple linear regression model for Multiple Sclerosis Quality of Life-54 scores where patient groups are constant factor

Variables	Constant	Sex	Age	Marital status	Disease duration	EDSS	Adjusted r^2 (%)
Physical functioning	88.57*	−1.83	−0.944*	2.66	0.32	0.16	14.5
Role limitations due to physical problems	61.68	4.63	−0.6	10.61	0.9	0.78	10
Role limitations due to emotional problems	5.29	15.49	1.02	−16.9	−0.38	0.28	2
Bodily pain	35.57	5.34	−0.44	8.39	0.38	0.4	2
Emotional well-being	51.67*	0.12	−0.33	5.7	0.38	−0.35	−4
Energy	45.62*	0.66	−0.56	5.61	0.04	0.18	0.3
Health perception	74.18	2.37	−0.48	−2.91	0.23	0.23	−0.8
Social functioning	89.19*	1.43	−0.26	−2.03	−0.05	−0.1	−3
Cognitive function	64.26*	1.9	−0.28	3.46	−0.1	0.27	−6
Health distress	61.44	−4.87	−0.35	9.51	0.33	−0.02	−3
Sexual function	−90.9	9.13	−0.84	75.63*	1.27	−4.93	24
Change in health	42.77	−1.06	−0.18	−4.22	0.37	0.66	7
Satisfaction with sexual function	−52.94	−5.52	−0.22	52.3	1.37	−0.59	2
Overall quality of life	63.8*	2.1	−0.79*	12.07*	0.46	0.04	−0.3
Physical health	61.06	0.54	−0.36	9.62	0.67	−7.57*	38
Mental health	45.98	3.73	−0.09	1.62	0.14	0.01	−5

Each regression model was adjusted for sex, age, marriage, diagnosis duration, and EDSS. *$P<0.05$. EDSS=Expanded Disability Status Scale

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.

Conflicts of interest
There are no conflicts of interest.

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