

Comparison of the Effects of CinnoVex, Rebif and Betaferon on a Expanded Disability Status Scale of Patients With Multiple Sclerosis

Nastaran Madjdinasab^{1,*}; Seyed Ehsan Mohammadiany Nejad¹; Shahram Tarahomi¹; Fatemeh Sadr¹; Mohammad Bahadoram¹

¹Department of Neurology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran

*Corresponding author: Nastaran Madjdinasab, Department of Neurology, Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran. Tel: +98-9163116496, E-mail: n.madjdinasab@gmail.com

Received: November 12, 2014; Accepted: December 28, 2014

Background: Multiple Sclerosis (MS) is the most common chronic inflammatory autoimmune disease of central nervous system that is characterized by demyelination and loss of axons. The most common criterion for assessing disability in patients is the Expanded Disability Status Scale (EDSS), which is calculated based on the presence or absence of neurologic side effects. The beta interferons are effective drugs in preventing the recurrence of attacks and disease progression. Three types of beta interferons are used in the treatment of MS: CinnoVexR, Rebif and Betaferon.

Objectives: This study aimed to compare the effects of CinnoVex, Rebif and Betaferon on the EDSS of patients with MS.

Patients and Methods: In this study, a total of 92 patients with Relapsing-Remitting Multiple Sclerosis (RRMS) were randomly allocated into three equal groups; each treatment group received one of the foregoing drugs (CinnoVexR, Rebif and Betaferon) for one year. At the beginning and end of the study, patients' EDSS was measured and compared.

Results: In this study, the relative frequency of female to male gender was 85.71% versus 14.21% and the mean age of the patients was 28.21 years. Following taking medication, patients' EDSS showed a significant increase in all three groups during a year. However, no significant difference was observed regarding the average increase of patients' EDSS among three groups of patients at the beginning and end of the study.

Conclusions: It seems that CinnoVex, Rebif and Betaferon do not have a significant difference in reducing disability in patients with MS after 12 months. According to the findings of this study, no significant difference was observed in reducing disability in MS patients among the three groups (CinnoVex, Rebif and Betaferon) after 12 months.

Keywords: Multiple Sclerosis; Betaferon; Rebif

1. Background

Multiple Sclerosis (MS) is an inflammatory disease of the central nervous system, which is characterized by destruction of myelin in the brain and spinal cord. This disease is chronic; it mostly happens at the ages of 20 to 40 years and its prevalence in women is more than men (1, 2). The symptoms of the disease are very diverse, depending on the central nervous system involvement place, as sensory-motor expressions, the brain stem, sphincteric and cognitive problems (3). Currently, the most common scale for assessing the disability of patients is the Expanded Disability Status Scale (EDSS) (4-6), which is calculated based on the presence or absence of neurologic side effects (cranial nerves, sensory and motor systems, the control of sphincter, etc.). This scale in perfectly normal persons is changing from zero (normal neurologic status) to ten (death due to MS). Medications that are used nowadays in the treatment of MS are prescribed to control the symptoms during the

attacks and prevent the recurrence of the disease (2). Beta interferons are approved drugs for preventing recurrence of the attacks and are disease modifiers (2). Three types of beta interferon in the treatment of MS are used: interferon beta 1a (AVONEX), interferon beta 1a (Rebif), interferon beta 1b (Betaferon) (1). All of these drugs are effective on the rate of recurrence, progression of disability and MRI findings of MS patients, but do not have a significant impact on primary progressive MS (PPMS) (1).

2. Objectives

According to the unknown superiority of any one of the three above-mentioned drugs in reducing the amount of patients' disability, this study was designed to compare the extent of the impact of each of these three drugs on the EDSS scale of treated patients.

3. Patients and Methods

In this clinical trial, the MS patients referred to the neurology clinic of Ahvaz Golestan Hospital were selected according to the inclusion criteria as follows: The definitive diagnosis of MS by two different neurologists based on the 2010 McDonald's criteria (based on clinical examinations, brain and cervical Magnetic Resonance Imaging (MRI) and the tests for rule out the other diseases), age between 15 to 45 years, lack of other neurologic diseases, the lack of the use of any type of interferon for more than a month before the study, EDSS of the study start equal to or less than 5.5. The exclusion criteria were the PPMS patients, severe hepatic disorders (AST or ALT more than three times of the normal limit), cytotoxic drug intake during the six months prior to the study, pregnancy and lactation, intolerance to interferons. CinnoVex (AVONEX, SINAGEN Co) with a dose of 30 mcg/IM/weekly, Rebif with a dose of 44 mcg/SC/3 times a week and Betaferon with a dose of 250 mcg/SC/qod, were used in this study. A total of 105 patients participated in this study were randomly allocated into three equal groups (n=35) and each group received one of the three drugs (CinnoVexR, Rebif and Betaferon). Patients' EDSS was measured at the beginning and twelve months after the start of the study. To analyze the data, the independent t-test, paired t-test, ANOVA, and SPSS version 19 software were used.

4. Results

The mean age of the patients participated in the study was 28.21 years. The participants' age range was between 16 and 47 years old. Ninety patients (85.71%) were female and 15 (14.29%) were male. During a twelve-month period of the study, five and eight persons due to change in their

medication (need for second line drugs-convert to the secondary progressive MS), and a lack of adherence to the plan were excluded from the study, respectively. The exclusion of these cases did not have a significant impact on the statistical results. No significant difference was observed in terms of gender and age distribution of the participants among the three drug groups (Table 1). Patients' EDSS in each of the three groups was measured and compared with the ANOVA test that no significant difference was seen among the groups. After twelve months, the participants' EDSS was measured again and compared (Table 2). Paired t-tests showed that the rate of patients' EDSS was increased in all the pharmaceutical groups significantly within one year. Then ANOVA was performed to test the difference in the average increase for EDSS between three groups (Table 3). As it can be seen, no significant difference was found in the average increase of EDSS among the three pharmaceutical groups at the end of the twelfth month.

5. Discussion

Multiple sclerosis is the most common chronic inflammatory autoimmune disease of central nervous system that is characterized by demyelination and loss of axons (6, 7), and due to the lack of access to the definitive treatment for it, different treatments are used to control it. In this study, the effectiveness of three drugs CinnoVex, Rebif and Betaferon has been compared through the assessment of patients' EDSS at the beginning of the study and twelve months later. In this study, the average age of patients was lower than previous studies (1, 8). In this study, the relative frequency of female to male gender was more than previous studies (7, 8).

Table 1. Frequency (and Relative Frequency) of the Participants in the Project by Separation of Sex and Incoming Drug Type

| Gender | Study Group (Relative Frequency) | | | |
|--------|----------------------------------|------------|------------|------|
| | CinnoVex | Rebif | Betaferon | EDSS |
| Male | 4 (12.9) | 4 (13.34) | 4 (12.91) | 1.20 |
| Female | 27 (87.09) | 26 (86.66) | 27 (87.09) | 1.19 |

Table 2. Comparison of the Amount of Recipients' EDSS for Each Interferon, at the Beginning and End of the Study

| | EDSS: Beginning of the Study | EDSS: End of the Study | EDSS Difference: Beginning Versus End | P Value |
|-----------------|------------------------------|------------------------|---------------------------------------|---------|
| All of patients | 1.19 | 2.14 | 0.048 ± 0.14 | 0.022 |
| CinnoVex group | 1.11 | 2.17 | 0.057 ± 0.21 | 0.018 |
| Rebif group | 0.93 | 1.97 | 0.04 ± 0.11 | 0.016 |
| Betaferon group | 1.45 | 2.55 | 0.15 ± 0.20 | 0.011 |

Table 3. Comparison of the Difference in Average Increases of EDSS Between Three Groups Receiving CinnoVex, Rebif and Betaferon: The End of the Twelfth Month

| Between Groups | Sum of Squares | df | P Value |
|----------------|----------------|----|---------|
| | 4.25 | 2 | 0.24 |

The results of previous studies on different drugs are different. A study showed that the CinnoVex can prevent the progression of disability in patients with MS, and even in some cases it has reduced disability (2). Also, studies have shown that Rebif has a beneficial effect on the rate of relapse and lesions from MRI in MS patients' brain compared to placebo (4). In another study, the annual rate of recurrence in the MS patients treated with Betaferon for one year decreased 35%. In a survey the annual rate of recurrence in 63 MS patients treated over a period of 18 months with AVONEX was associated with a decrease in attacks; however, the age of the patients did not have a role in the outcome of the treatment (3). Each of the three types of interferon (AVONEX, Rebif and Betaferon) has the same effects equivalent to a 30% relapse reduction in MS attacks in the patients (9-11). In one study, the significant effect of these drugs was represented in reducing the recurrence and EDSS (12). A study of the efficacy of three drugs of AVONEX, Rebif and Betaferon in reducing relapses and EDSS did not find significant differences in reducing relapses and EDSS among patients receiving these three drugs (1). In accordance with the available references (1, 6), this study also did not show any significant difference in the average of the differences of EDSS of the patients in three pharmaceutical groups at the end of the study (9) (Table 3); basis on the findings of this study, CinnoVex, Rebif and Betaferon have no significant difference in reducing disability in MS patients. This may be according to the similar mechanism of action, a short-time period of the study, or small study group. Limitations of the study were the short time of the study and a small sample size. It is recommended that this study be done with a larger sample size and at a longer period of time.

Acknowledgements

We would like to thank Eisa Motaharitarab, Majid Teimuri Rad and Samira Mardaniyan for their help in collection and analysis of data.

References

1. Mazdeh M, Afzali S, Jaafari MR. The therapeutic effect of Avonex, Rebif and Betaferon on EDSS and relapse in multiple sclerosis: a comparative study. *Acta Med Iran.* 2010;**48**(2):83-8.
2. 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 Sci.* 2010;**68**(1):30-6.
3. Weinstock-Guttman B, Bakshi R. Combination therapy for multiple sclerosis: the treatment strategy of the future? *CNS Drugs.* 2004;**18**(12):777-92.
4. Ebers GC. Randomised double-blind placebo-controlled study of interferon β -1a in relapsing/remitting multiple sclerosis. *Lancet.* 1998;**352**(9139):1498-504.
5. Pozzilli C, Prosperini L, Sbardella E, De Giglio L, Onesti E, Tomasini V. Post-marketing survey on clinical response to interferon beta in relapsing multiple sclerosis: the Roman experience. *Neurol Sci.* 2005;**26**(4):s174-8.
6. Olek MJ, Dawson DM. Neurology in Clinical Practice. In: Bradley GW, Daroff R. B. , Fenichel G. M. , Jankovic J editors. *Multiple sclerosis and other inflammatory demyelinating diseases of the central nervous system.* 4th ed. Philadelphia: Butterworth & Heinemann; 2004. pp.1631-64.
7. Cottrell DA, Kremenchutzky M, Rice GPA, Koopman WJ, Hader W, Baskerville J, et al. The natural history of multiple sclerosis: A geographically based study. *Brain.* 1999;**122**(4):625-39.
8. Kremenchutzky M, Cottrell D, Rice G, Hader W, Baskerville J, Koopman W, et al. The natural history of multiple sclerosis: a geographically based study. 7. Progressive-relapsing and relapsing-progressive multiple sclerosis: a re-evaluation. *Brain.* 1999;**122** (Pt 10):1941-50.
9. IFNB Multiple Sclerosis Study Group . Interferon beta-1b is effective in relapsing-remitting multiple sclerosis I. Clinical results of a multicenter, randomized, double-blind, placebo-controlled trial. *Neurol.* 1993;**43**(4):655.
10. Jacobs LD, Cookfair DL, Rudick RA, Herndon RM, Richert JR, Salazar AM, et al. Intramuscular interferon beta-1a for disease progression in relapsing multiple sclerosis. The Multiple Sclerosis Collaborative Research Group (MSCRG). *Ann Neurol.* 1996;**39**(3):285-94.
11. Claire SR, Mark JT. Demyelinating Diseases. In: Lewis PR, Timothy AP editors. *Merritt's Neurology.* Philadelphia: Lippincott Williams & Wilkins; 2005. pp. 958-60.
12. Etemadifar M, Janghorbani M, Shaygannejad V. Comparison of Betaferon, Avonex, and Rebif in treatment of relapsing-remitting multiple sclerosis. *Acta Neurol Scand.* 2006;**113**(5):283-7.