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ORIGINAL ARTICLE

Report of the Multiple Sclerosis Treatments in Iran (Khorasan Provinces)

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ABSTRACT

Multiple sclerosis (MS) is a chronic disease of the central nerve system. Iran has a medium-high prevalence of MS patients. While much is known about the beneficial and adverse treatments of MS in the world, there is a paucity of documental information about MS treatments in Iran. This study was done to provide the documentary details of MS medications. In a 6-month cross-sectional study, 248 MS patients from the Mashhad MS association in the Khorasan province were surveyed. Data was collected by employing a 32-item self-administered questionnaire in a face to face interview, which consisted of different variables. Nonparametric tests and descriptive statistical analysis were applied to assess the distribution and the effects of medication use in the population. 40% of the patients used interferonß-1b (Betaferon), 30% used interferonß-1a (Rebif), 14% used interferonß-1a (Avonex), 13% used interferon ß-1a (CinnoVex) [Immunomodulatory Agents (IMDs)] and 3% used Mitoxantrone (Non-IMDs). The patients' satisfaction with INF therapy in terms of, the most efficacy, the least side effect, the cost and attacks reduction was 59% for Avonex, 74% for Betaferon, 44% CinnoVex and 77% for Rebif. The most adverse effects reported by Avonex users were flulike symptoms (53%), headache (31%), tiredness and muscle-aches (16%); Betaferon: flulike symptoms (60%), injection site reactions (25%), hair loss(15%) and Rebif: headache and muscle-aches (60%), injection site reactions (30%) and menstrual disorders (10%) . There was no significant association between the side effects of INF with respect to gender, the war attendance, family history of attending in the war, BMI (p value>0.05). The only significant difference was between CinnoVex side effects with respect to gender and BMI, as a high proportion of females reported flu-like symptoms, injection site reaction and hair loss. The common method of MS treatment was the modulation of the immune system with IMDs, low-dose (Avonex-CinnoVex) for low frequency and high -dose (Betaferon-Rebif) for high frequency. The main aim of symptom therapy was to cure depression and spasticity. The least adverse effects were related to Rebif, Betaferon, and Avonex respectively. The only medicine for MS relapses was a course of high dose of Methyl prednisolone. The overall treatment pattern of MS in Iran is like that in the western countries.

Key Words: multiple sclerosis, pharmacoepidemiology, Iran

Key Message: To accomplish comprehensive of MS studies need to provide an estimate of the probability of the beneficial effects, or the probability of the adverse effects in populations and other parameters relating to drug use may benefit from using epidemiological studies. Then, the application of epidemiological methods to pharmacological approaches may be explained as Pharmacoepidemiology [5].

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Introduction

The aim of treatment in patients with MS is to delay the onset of disability, return function after an attack, reduce the frequency of attacks, treat the symptoms and prevent or delay the disability. Six Immunomodulatory Agents (IMAs) have been approved by FDA (The US Federal Drug Administration) for use in MS therapy: Interferon beta-1b, (Betaseron,), Interferon beta-1a (Avonex), Glatiramer acetate (GA, Copaxone), Mitoxantrone (Novantrone), Interferon beta-1a (Rebif) and Tysabri (Natalizumab). .MS relapses can best be treated with a course of high dose intravenous methylprednisolone (500 mg) [1],[2],[3] and CinnoVex (Interferon betai1a), which has approved either inside Iran or in Europe [4].

Material and Methods

This study took place within six months in the Khorasan MS association, a Non –Governmental Organization in the province of Razavi Khorasan. The Khorasan provinces (Razavi Khorasan, Northern Khorasan, and Southern Khorasan) are located in the northeast of Iran, with a population of 5600000. The study subjects were members of the MS association in Mashhad. The Multiple Sclerosis registry consisted of 693 members. We selected a random sample of 248 Multiple Sclerosis patients. The eligible patients were men and women who had clinically or laboratorily supported definite MS according to the McDonald criteria (revised 2005) [6]. The patients were excluded if they had neurological illness apart from MS or any other acute or chronic disease. To study the pharmacoepidemiology of MS, first line therapy, symptom therapy and pulse therapy, all the patients asked for the prescription medicine. The MS survey was in the field from 12th July 2008 to 12th January 2009.The survey was completed by 258 individuals. Of the 258 patients, 12 had missing data for some items. The analysis was based on the remaining 248 participants. Their ages were grouped into 10-year intervals, i.e. 10-19, 20–29, 30–39 and ≥40 years.

Results

Out of the 248 Multiple Sclerosis patients, 240 (96.8%) were prescribed the Interferons (INFs) as an immunomodulating agents, with a Relapsing Remitting course of MS. Only 8 (3.2%) patients were prescribed Mitoxantron as a non-Immunomodulating agent (Mitoxantron is an Immunosuppressant) with a Secondary Progressive and a Primary Progressive course of MS. The total patients were prescribed Corticosteroids for spiking the attacks. A typical prescription for spiking the attacks included intravenous Methyprednisolon 500mg, vial N=14; Dextrose water 500cc serum, N=7 and Prednosolon 50 mg tablet N=60. 18.6% of the patients were prescribed the medicines. (e.g. Baclofen, Clonazepam, Amantadin, Floxetin Oxybutinine and Valproate sodium) as symptom therapy for treating the spasticity, tremor, fatigue, sexual dysfunction, depression, bladder and bowel dysfunction and paroxysmal symptoms as the common MS symptoms. There were 33 patients below 18 years who were prescribed Interferon and some individuals were unable to walk (EDSS ≥5.5) but were prescribed INFs. The results of this study showed that 12.8% of the patients (33 individuals) were ineligible for treatment with Interferons [7]. Thirty four patients (13.7%) used Avonex once a week (IM) each dose of which costed $100; up t o 100 patients (40.7) took Betaferon every other day (SC) with a cost of $ 55 per dose; 32 (13%) individuals used CinnoVex once a week (IM) each dose of which costed $50 and up to 29% of the patients (73) were prescribed Rebif every other day (SC) with a cost of $ 55 per dose. Only 8 (3.2%) patients used Mitoxantrone, every three months (IV) with a cost of $ 58 per

dose. Our survey results indicated that 41 percent of Avonex consumers reported adverse drug reactions. Twenty six percent of Betaferon consumers confirmed the side effects after taking Betaferon. Among CinnoVex consumers, 53% of the patients reported ADRs. Our findings proved that 23% of the Rebif consumers showed adverse reactions. These side effects are stated in Table 1.The results revealed that the patients' satisfaction with Interferon therapy in terms of, the most efficacy (delay the onset of disability and reducing the frequency of attacks), the least side effect and the cost of the MS treatment was 59% for Avonex, 74% for Betaferon, 44% for CinnoVex and 23% for Rebif. The results of the three Interferons (INFs) showed that there was no significant association between the side effects of the Interferons with respect to gender and BMI (Body Mass Index) group (p value>0.05). The only significant difference was between CinnoVex side effects with respect to gender and BMI groups, as a high proportion of females reported flu-like symptoms, injection site reaction, and hair loss.

Discussion

Many countries have their own strategy and guidelines for the treatment of MS. According the Iranian Guidelines for MS management which is prepared by the National MS Committee and the Ministry of Health of Iran (MOH), Interferons are prescribed in specific conditions including Relapsing Remitting MS, active MS (that is diagnosed by MRI or Clinical symptoms), EDSS (Expanded disability status scale as an evaluation tool for the effects of MS [8] medicine) ≤ 5.5, without any contraindications. INFs cannot be indicated in SPMS without replaces, but can be considered in SPMS with relapse [9]. Disease –modifying agents are generally prescribed for individuals with PPMS or SPMS in the US (1) and IMDs are contraindicated for patients below 18 years [10]. INFs are occasionally prescribed for PPMS and for below 18 years old patients. The neurologists believed that a sociocultural approach in disease treatment was the only reason which forced them to prescribe unnecessary treatments. Despite the Iranian guidelines and the English Guidelines, 12.8% of the patients were prescribed INFs.. In addition to immunomodulation and immunosuppression, the special treatment of the symptoms is a significant aspect of the overall management of multiple sclerosis. The majority of the medicines which are used as symptomatic treatments are Acetaminophen and Brufen (flu-like symptoms related to INFs)), Sodium Valproate (paroxysmal symptoms) , Clonazepam and Lorazepam (tremor and insomnia) Carbamazepine (Tremor) and Oxybutinine (bladder dysfunction) which is aimed at the elimination or decrease of symptoms which impair the functional abilities and the quality of life of the MS individuals [11],[12]. Nevertheless, the overall treatment pattern of MS in Iran is similar to that in the western countries. Although the most adverse effect reaction was related to CinnoVex, that forced the patients to break off or to change the medicine, the flu-like symptoms as the most common adverse reactions of INFs among the consumers of CinnoVex were very low. The side effects related to CinnoVex in females were more than the ones in males. Women are more likely to seek adverse drug reactions (ADRs) and hence the greater possibility of being involved with ADRs. On the other hand, CinnoVex had the least cost among the four INFs in our study. Hence, we expected the patients to completely accept the INFs, but the most satisfaction was seen with the use of Betaferon and Avonex. It might be related to the short–term marketing life of CinnoVex in comparison to the other INFs. CinnoVex is the trade mark of Interferon beta-1a which has been released into the market after passing through a long way of appropriate clinical trials and quality controls, either inside Iran or in Europe. It was accessible in the markets in 2007 [4], [13] . The higher education level of the MS patients is in agreement with others [14]. The educated youth in developing countries are most likely to accept a western lifestyle, and hence the risk of developing a western illness like MS [15]. Consequently, they prefer to use western medicine in comparison to local medicine.

Conclusion

Overall, the pattern of the treatment of MS in Iran is similar to that seen in western countries. INFs are prescribed as the first line therapy. Moreover, non- immunomodulating agents such as Mitoxantron are used in eligible MS patients and a high course of intravenous Methyl prednisolone (pulse therapy) is applied for spiking the attacks. Actually, the important protocol in MS treatments are; delaying the onset of disability, returning function after an attack , reducing the frequency of attacks and treating the symptoms . Further researches are needed to ascertain the pharmacoepidemiological aspects of multiple sclerosis.

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