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Factors associated with adherence to disease modifying therapy in multiple sclerosis: An observational survey from a referral center in Lithuania☆

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ABSTRACT

Aim of the study: To investigate adherence to disease modifying therapy (DMT) in Lithuanian population of multiple sclerosis patients and factors associated to it.
Methods: Patients receiving one of the following DMT's: Interferon β 1a (Rebif) 44 micrograms three times a week subdermally (s/c) or Interferon β 1a (Avonex) 30 micrograms weekly intramuscularly (i/m), or Interferon β 1b (Betaferon, Extavia) 250 micrograms once in two days s/c, or Glatiramer acetate (Copaxone) 20 mg daily s/c, were presented with a questionnaire inquiring their demographic and clinical characteristics and adherence to treatment profile, as well as HAD scale and SF-36 questionnaire. Those who missed at least one dose of DMT during last three months were considered non-adherent.
Results: In total, 207 patients were enrolled, 73 (35.3%) of them were non adherent during last three months. More patients with university education (p=0.004, χ^2 =8.466 high school/vocational *vs.* university) as well as consuming > 4 units/year of alcohol were non-adherent during last three months (p=0.005). Average score for anxiety (6.69 ± 4.03 *vs.* 6.92 ± 4.24) and depression (4.74 ± 3.9 *vs.* 4.7 ± 3.83) in HAD scale did not differ significantly between adherent and non-adherent groups. We did not find any significant difference in quality of life scores (SF-36 v.2) between the groups. No significant difference of adherence was found then comparing patients often suffering from drug side effects with those who experience rare or no side effects. In logistic regression model, patients consuming more than 4 alcohol units per year and patients with university education were more likely to miss at least one dose during last three months: 2.121 (95% CI: 1.143–3.937, p=0.017) and 2.409 (95% CI: 1.260–4.642, p=0.008) times accordingly. Patients with better quality of life scores were slightly less likely to be non adherent (OR 0.997 (95% CI: 0.994–0.999), p=0.0017).
Conclusions: One third of patients were non-adherent during last three months. Worse adherence rates were associated with higher education and higher alcohol consumption. Education, alcohol consumption and quality of life scores were found to be significant factors for predicting non-adherence. We found no associations between adherence and anxiety, depression, or drugs side effects.

1. Introduction

Multiple sclerosis (MS) is a chronic demyelinating and neurodenegerative disease of central nervous system, causing wide variety of neurological symptoms, including muscle weakness, spasticity, coordination disturbances, sensory deficits and pelvic organ dysfunction. With debilitating relapses and progression it is a leading cause of morbidity and disability in young adults (Lavery et al., 2014). MS affects individual wellbeing in form of deteriorating physical condition as well as mental state by increasing isolation, dependence, depression (Simmons, 2010). Furthermore, it brings economic burden to society by decreasing contribution of working age individuals, increasing their healthcare expenses (Lizán et al., 2014).

Adherence indicates the extent to which a person's behaviour: taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider (Burkhart and Sabaté, 2003). Patients with chronic diseases, including MS, have lower adherence compared to those with acute illness (Osterberg and Blaschke, 2005). Adherence to injectable disease modifying therapies (DMT) in MS is poor: 14–47% of patients

Abbreviations: DMT, disease modifying therapy; EDSS, expanded disability status scale; IFN, interferon

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Table 1
Patients' demographical and clinical characteristics.

Characteristics	n =207
Gender, n(%)	
Male	65 (31.4%)
Female	142 (68.6%)
Age, years (mean ± SD)	42.9 ± 10.1
Education, n (%)	
High school/vocational	92 (44.4%)
College	42 (20.3%)
University	73 (35.3%)
Marital status, n (%)	
Unmarried	44 (21.3%)
Married	114 (55.1%)
Divorced	40 (19.3%)
Other	9 (4.3%)
Employment status, n (%)	
Employed	93 (44.9%)
Unemployed	114 (55.1%)
Occupational disability, n (%)	
Confirmed	124 (59.9%)
Absent	83 (40.1%)
Alcohol consumption, n (%)	
≤4 units/year	115 (55.6%)
5 units/year–1 unit/month	63 (30.4%)
> 1 unit/month	29 (14%)
MS duration, years (mean ± SD)	8.2 ± 4.1
Age on MS onset, years (mean ± SD)	35.0 ± 10.0
EDSS on the survey day, n (%)	
< 3 points	124 (59.9%)
≥ 3 points	83(40.1%)
Exacerbations during last 2 years (mean ± SD)	0.7 ± 0.8
Overall DMT duration, years (mean ± SD)	5.0 ± 2.7
Duration of current DMT medication use, years (mean ± SD)	4.4 ± 2.7
DMT medication, n (%)	
IFN β 1a 3x week s/c	73 (35.3%)
IFN β 1a 1x week i/m	37 (17.9%)
IFN β 1b 1x two days s/c	40 (19.3%)
Glatiramer acetate 1 x day s/c	57(27.5%)
Previous treatment with other DMT, n (%)	
Yes	34 (16.4%)
No	173 (83.6%)

discontinue their treatment during first 2–8 years (Devonshire et al., 2011).

Although multiple sclerosis is currently not curable, there are several DMTs confirmed for MS treatment and this number is growing. It is widely accepted that DMTs bring numerous benefits for MS patients: reduce relapse frequency (Lizán et al., 2014), hospitalisation rates (Remington et al., 2013), disease progression (Menzin et al.). On the other hand, it might be difficult for patients to adhere to treatment that is long term, usually unpleasant, requiring self-injecting and not showing an immediate effect on one's wellbeing (Di Battista et al., 2014). In order to improve adherence, understanding the reasons for disregarded regimen is of utter importance.

Various studies in the last decade determined a number of factors contributing to DMT adherence in MS. Devonshire and colleagues showed that feminine gender, shorter disease and treatment duration as well as better quality of life are associated with better adherence to DMT (Devonshire et al., 2011). According to study carried out by Treadaway, patients who were older at the onset of disease had shorter disease duration than three years and were treated with the first DMT were more adherent to therapy (Treadaway et al., 2009). Furthermore, alcohol consumption has negative effect on adherence (Tremlett and Oger, 2003). Factors like anxiety, depression, belief in treatment efficacy, sufficient information about disease and treatment are associated with adherence (de Seze et al., 2012; Fraser et al., 2003; Mohr et al., 2001; Treadaway et al., 2009).

Medications for first line MS treatment in Lithuania are: Interferon β 1a 44 μg (*Rebif*), Interferon β 1a 30 μg (*Avonex*), Interferon β 1b 250 μg (*Betaferon, Extavia*), and Glatiramer acetate 20 mg (*Copaxone*) To our best knowledge, there are no previous publications concerning adherence to DMT regimens in Lithuania. Thus, the aim of our study was to determine factors, associated with adherence to injectable DMTs in MS in Lithuanian population.

2. Methods

An observational study was carried out in Lithuanian University of Health Sciences Hospital Kaunas clinics, Neurology outpatient clinic (which is one of three MS referral centers in Lithuania) from October 2012 to March 2013. Inclusion criteria: consecutive adult Neurology clinic outpatients, diagnosed with confirmed relapsing-remitting multiple sclerosis with EDSS lower than 6 points and receiving one of injectable DMTs: Interferon β 1a (*Rebif*) 44 micrograms three times a