Predictors of adherence using panel survey data from multiple sclerosis patients currently treated with high–dose, high–frequency interferons

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Introduction

- Multiple sclerosis (MS) is a chronic, inflammatory-mediated, neurodegenerative disease that results in a variety of symptoms, including walking and coordination problems and cognitive impairment.[1,2]
- Relapsing–remitting MS (RRMS) is characterized by the occurrence of defined attacks or relapses that result in the worsening of neurological function, with partial or complete recovery between each attack.[1,2]
- Several disease-modifying drugs (DMDs) have been developed to reduce relapse frequency and delay disability progression.
- High-dose, high-frequency beta interferons (IFNs) are an effective treatment option for patients with relapsing MS, with proven long-term safety and tolerability profiles.[1]
- Suboptimal adherence to DMD regimens is common in MS.[1]
- DMD adherence is associated with lower relapse rates.[3,4]

Objective

- To investigate patterns of treatment adherence in patients with MS treated with high-dose, high-frequency IFNs.

Methods

- A database of 1000 patients with MS was created from a random sample of 969 patients from the US National Health and Wellness Survey[5] or Lightspeed Research panel who completed an internet survey between November and December 2012, augmented with 31 patients who were required to ensure the sample contained a minimum of 100 patients with current oral therapy.
- The survey contained demographic, disease characteristic, and healthcare experience variables.
  - The Patient-Determined Disease Steps (PDDS) questionnaire was used as one of the measures and is a patient-reported outcome of disability in MS.[6]
- Respondents were included in the analysis if they were aged ≥18 years, were clinical trial–naïve, had RRMS, and were, at the time of the survey, receiving subcutaneous IFN beta-1a (sc IFN β-1a) three times weekly (tiw) or sc IFN β-1b every other day (eod) and indicated use for ≥4 months (ie, to ensure a minimum exposure to the current therapy).

- Adherence was measured using the 4-item Morisky Medication Adherence Scale (MMAS-4),[7] shown in **Table 1**.
  - MMAS-4 is a self-reported measure of medication-taking behavior.
  - The MMAS-4 instrument has been shown to be a valid self-reported measure.[7]
  - Patients score one point for every 'Yes' answer. A score of 0 indicates high adherence; a score of 1 or 2 indicates intermediate adherence; and a score of 3 or 4 indicates low adherence.

Table 1. Items and scoring for the MMAS–4 scale.[2]

Question number	Question	Valid responses
1	Do you ever forget to take your medicine?	Yes or No
2	Are you careless at times about taking your medicine?	Yes or No
3	When you feel better do you sometimes stop taking your medicine?	Yes or No
4	Sometimes if you feel worse when you take the medicine, do you stop taking it?	Yes or No

Scoring: score one point for every 'Yes' answer. A score of 0 indicates high adherence; a score of 1 or 2 indicates intermediate adherence; and a score of 3 or 4 indicates low adherence.
MMAS-4, 4-item Morisky Medication Adherence Scale.

- Patients were categorized as 'high' adherers (negative response to all four questions) or 'intermediate/low' adherers (any positive response).
- Logistic regression analysis was used to determine the association among the survey variables and adherence category, controlling for covariates. A significance level of p<0.1 was selected to determine potential predictors of adherence. Variables meeting this requirement are presented here.
- For the descriptive tables comparing patients treated with sc IFN β-1a versus those treated with sc IFN β-1b, continuous measures were tested with independent two-sample *t*-test, and categorical measures were tested with chi-square or Fisher's exact tests (for cell size <5).
- All analyses were conducted using SAS 9.4 for Windows (Cary, NC, USA).

Results

- Of 969 surveyed, 80 sc IFN β-1a and 63 sc IFN β-1b patients met inclusion criteria (mean [standard deviation] age: 49.0 [10.4] years, 88.8% female, vs 51.3 [8.7] years, 87.3% female, respectively; p values >0.05; **Table 2**).
- The proportions of respondents treated with sc IFN β-1a or sc IFN β-1b who responded 'Yes' to each item on the MMAS-4 are shown in **Figure 1**.
  - The questions with the highest percentages of patients responding affirmatively were "Do you ever forget to take your medicine?" and "Are you careless at times about taking your medicine?"

Table 2. Sample attrition.

Criteria	Patients removed, n	Patients remaining, n
Total number of subjects in the database	NA	1000
Remove subjects who were not part of the random sample (ie, patients were added to the random sample to ensure that at least 100 patients using oral therapy were included)	31	969
Retain patients who report current use of sc IFN β-1a or sc IFN β-1b	790	179
Retain patients who have RRMS	15	164
Exclude patients with <4 months of exposure to current therapy (as the MMAS-4 scale asks specifically about the current therapy, patients are required to have ≥4 months of exposure to the current therapy)	5	159
Exclude subjects who have ever participated in a clinical trial	16	143[a]

IFN β, interferon beta; MMAS-4, 4-item Morisky Medication Adherence Scale; NA, not applicable; RRMS, relapsing–remitting multiple sclerosis; sc, subcutaneous.
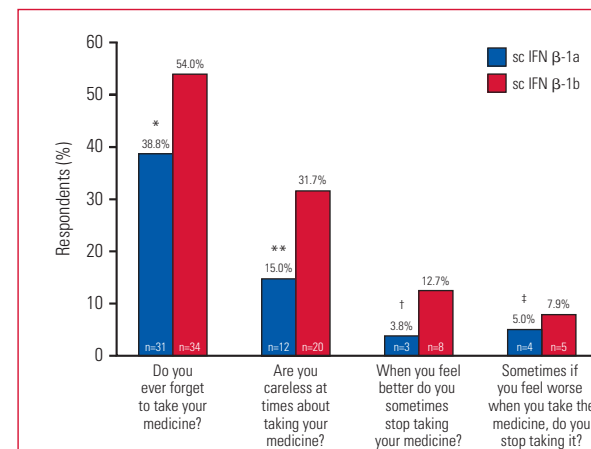[a]Number of patients who met the analysis criteria; 80 sc IFN β-1a patients and 63 sc IFN β-1b patients.

Figure 1. Number and percentage of respondents with 'Yes' response by MMAS–4 items.

Respondents could have indicated 'Yes' to more than one question.
IFN β, interferon beta; MMAS-4, 4-item Morisky Medication Adherence Scale; sc, subcutaneous.
*p=0.0696; **p=0.0171; †p=0.0600; ‡p=0.0574. Tests were chi-square or Fisher's exact if the cell size was <5.

- The percentages of respondents by MMAS-4 score (score of 0, 1, 2, 3, or 4) are shown in **Figure 2**.

Scoring: score one point for every 'Yes' answer. A score of 0 indicates high adherence; a score of 1 or 2 indicates intermediate adherence; and a score of 3 or 4 indicates low adherence.
IFN β, interferon beta; MMAS-4, 4-item Morisky Medication Adherence Scale; sc, subcutaneous.
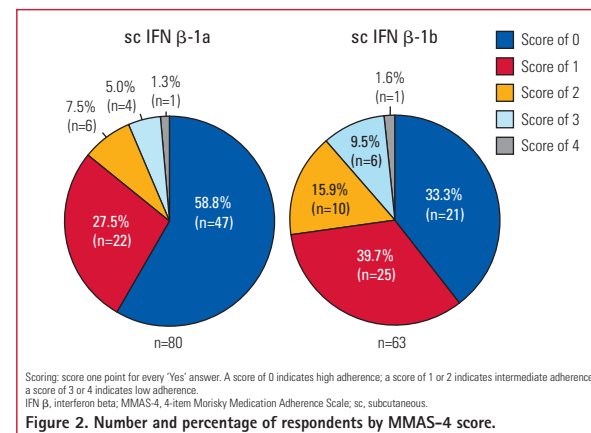Figure 2. Number and percentage of respondents by MMAS–4 score.

- The numbers and proportions of patients in each MMAS-4 category (high, score of 0 or intermediate/low, summed scores of 1, 2, 3, and 4) are reported in **Table 3**.
  - A greater percentage of sc IFN β-1a patients reported high adherence compared with sc IFN β-1b patients (58.8% vs 33.3%, p=0.0025).

Table 3. Number and percentage of respondents by adherence categories.

Adherence category	sc IFN β-1a n	sc IFN β-1a %	sc IFN β-1b n	sc IFN β-1b %	p value[a]
High (score of 0)	47	58.8	21	33.3	0.0025
Intermediate/low (summed score of 1, 2, 3, and 4)	33	41.3	42	66.7	
Total	80	100.0	63	100.0	NA

IFN β, interferon beta; NA, not applicable; sc, subcutaneous.
[a]Chi-square or Fisher's exact test if cell size is <5.

- Logistic regression model results are shown in **Table 4**.
  - After adjusting for covariates, sc IFN β-1a patients had greater odds of high adherence (odds ratio [OR] 2.92; p=0.0101).
  - Among the covariates, male sex (OR 4.37; p=0.0297), time since last relapse (years; OR 1.04; p=0.0483), frequent exercise (OR 1.06; p=0.0094), and PDDS score (OR 1.34; p=0.0110) were predictive of high adherence.
  - Age, time on current therapy, out-of-pocket expenditure/month, satisfaction, and importance to the patient regarding how effective the drug is at preventing magnetic resonance imaging lesions were not significant predictors of adherence.

Table 4. Predicting the odds of adherence using an indicator for current use of sc IFN β–1a versus sc IFN β–1b.

Model term	Standardized estimate	p value	Odds estimate	95% CI
sc IFN β-1a (sc IFN β-1b reference, Y/N)	0.294	0.0101	2.916	1.310, 6.743
Age (10-year increments)	0.060	0.6135	1.118	0.725, 1.735
Sex (reference female)	0.264	0.0297	4.368	1.246, 18.721
Time on current therapy (months)	−0.207	0.1096	0.994	0.986, 1.001
Time since last relapse (years)	0.287	0.0483	1.042	1.003, 1.090
Out-of-pocket expenditure/month ($10 increments)	0.038	0.6983	1.002	0.989, 1.020
Satisfaction (1 [least] to 7 [most] scale; 1-point increments)	0.219	0.0653	1.360	0.989, 1.911
Importance to the patient regarding how effective the drug is at preventing MRI lesions (allocation of 100 points over 9 categories; per 11.1-point increments[a])	0.079	0.4968	1.014	0.973, 1.058
Days in past month with ≥20 minutes of exercise (per day reference)	0.305	0.0094	1.060	1.016, 1.109
PDDS score (1 to 8; 1-point increments where higher scores represent greater disability)	0.322	0.0110	1.344	1.079, 1.707

CI, confidence interval; IFN β, interferon beta; MRI, magnetic resonance imaging; PDDS, Patient-Determined Disease Steps; sc, subcutaneous.
[a]11.1 points represents the number of points that would be allocated if each of the 9 points were perceived as equal.

Conclusions

- In this exploratory analysis, treatment with sc IFN β-1a tiw was strongly associated with high adherence relative to sc IFN β-1b eod.
  - A higher proportion of patients receiving sc IFN β-1a were categorized as being adherent to treatment, compared with those treated with sc IFN β-1b.
- The findings suggest that in patients with RRMS receiving sc IFN β-1a tiw or sc IFN β-1b eod, suboptimal adherence is most likely to be due to the patient forgetting to take, or being careless about taking, his or her medication.[1]

References

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Acknowledgments

Disclosures

To view the ePoster, scan the QR code or go to http://medpub-poster.merckgroup.com/CMSC2015_DX45.pdf

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