Adherence to laboratory monitoring among people taking oral drugs for multiple sclerosis: a population-based study

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Background

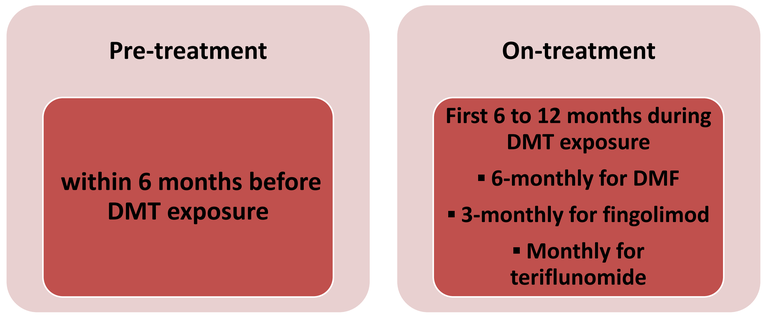
- The oral disease-modifying therapies (DMTs) for multiple sclerosis (MS) are associated with improved drug adherence relative to the injectable DMTs.
- There is very little information on how well MS patients adhere to the blood and urine tests that are required for safety monitoring.

Objective

To examine adherence to laboratory testing by persons initiating an oral DMT for MS.

Methods

- Linked, population-based health administrative and laboratory data were accessed (see **Sources of data**).
- *Population*: All persons in British Columbia, Canada, who filled their 1st prescription for **dimethyl fumarate (DMF), fingolimod or teriflunomide,** in 2011-2015.
- Adherence to each drug monograph's recommended laboratory monitoring requirements was assessed for lymphocyte counts, liver enzyme levels, and urine protein within specific time intervals pre- & on-treatment.



- The **association between patient characteristics and adherence** was examined using multivariable logistic regression and the generalized estimating equations.

Sources of data

Health administrative data were accessed to extract patient characteristics including sex, age, socioeconomic status, comorbidity burden measured using diagnosis codes from hospital and physician visits, and exposure to oral and non-oral DMT using prescription data.

Laboratory data were accessed from sources that, combined, capture approximately 99% of laboratory tests in British Columbia (BC): LifeLabs Medical Laboratory Services (the largest community laboratory service provider in BC), Providence Health Care Society, the Provincial Health Services Authority, and each of the regional Health Authorities (HAs) in BC (Vancouver Coastal HA, Vancouver Island HA, Fraser HA, Interior HA, and Northern HA).

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Results

Table A. Proportions of people adherent to the recommended laboratory test

Number (n) of people included, by oral DMT and time period	Number & Proportion of people with a laboratory test					
	Biochemical liver test[a]		Lymphocyte count		Urinalysis	
	n	%	n	%	n	%
Dimethyl fumarate						
Pre-treatment						
Within 6 months, n= 567	518	91.4	531	93.7	438	77.2
On-treatment						
Months 1-6, n= 339	302	89.1	305	90.0	253	74.6
Months 7-12, n= 197	175	88.8	180	91.4	141	71.6
Fingolimod						
Pre-treatment						
Within 6 months, n= 253	222	87.8	231	91.3	NA	NA
On-treatment						
Months 1-3, n= 225	138	61.3	NA	NA	NA	NA
Months 4-6, n= 206	139	67.5				
Months 7-9, n= 192	118	61.5				
Months 10-12, n= 167	92	55.1				
Teriflunomide						
Pre-treatment						
Within 6 months, n= 196	179	91.3	183	93.4	NA	NA
On-treatment						
Month 1, n= 174	70	40.2	NA	NA	NA	NA
Month 2, n= 156	64	41.0				
Month 3, n= 147	59	40.1				
Month 4, n= 131	45	34.4				
Month 5, n= 124	39	31.5				
Month 6, n= 117	29	24.8				

[a]Minimum recommendations, for the biochemical liver tests, according to each DMTs product monograph: either ALT or AST for dimethyl fumarate and fingolimod; and for teriflunomide, either ALT or AST pre-treatment, and ALT while on-treatment.
NA – not applicable as the relevant laboratory test was not part of the routine monitoring recommendations.

Table B. Association between patient characteristics and adherence

Characteristics, by oral DMT	Adjusted Odds Ratio[a] (95% Confidence Interval)					
	Pre-treatment			On-treatment		
	Biochemical liver test	Lymphocyte count	Urinalysis	Biochemical liver test	Lymphocyte count	Urinalysis
Dimethyl fumarate						
Sex						
Female	Reference	Reference	Reference	Reference	Reference	Reference
Male	0.98 (0.50-1.94)	0.77 (0.36-1.64)	**0.61 (0.40-0.95)**	**0.46 (0.23-0.95)**	**0.47 (0.22-0.98)**	0.59 (0.35-1.01)
Pre-exposure to another DMT						
No	Reference	Reference	Reference	Reference	Reference	Reference
Yes	**2.71 (1.40-5.23)**	2.00 (0.97-4.14)	1.23 (0.82-1.87)	0.84 (0.41-1.72)	0.91 (0.43-1.90)	0.93 (0.56-1.54)
Fingolimod						
Sex						
Female	Reference	Reference	NA	Reference	NA	NA
Male	**3.50 (1.01-12.13)**	1.53 (0.48-4.86)		0.76 (0.49-1.17)		
Pre-exposure to another DMT						
No	Reference	Reference		Reference		
Yes	**2.69 (1.22-5.94)**	**3.96 (1.58-9.88)**		1.12 (0.71-1.78)		
Teriflunomide						
Pre-exposure to another DMT						
No	Reference	Reference	NA	Reference	NA	NA
Yes	**5.23 (1.28-21.41)**	**6.87 (1.27-37.13)**		1.14 (0.73-1.78)		

[a]The models were adjusted for sex, age, socioeconomic status, comorbidity score measured using the Deyo's adaptaion of the Charlson Comorbidity index in the baseline year, pre-exposure to other (non-oral) DMTs in the baseline year, and calendar year at the index date.
Bold indicates p<0.05. An odds ratio >1 indicates a higher likelihood, and an odds ratio <1 indicates a lower likelihood, of adhering to the monitoring schedule.
Other non-significant results are not presented in the table (including sex for teriflunomide; and age, socioeconomic status, and comorbidity for all the oral DMTs.)

Summary points

- The proportions of people adherent to pre-DMT liver and lymphocyte tests ranged from 88-91% and 91-94% respectively, while 77% adhered to pre-DMF urinalysis.
- Adherence to the first on-DMT liver test was 89% for DMF (within 6 months); 61% for fingolimod (within 3 months); 40% for teriflunomide (within 1 month).
- **Factors associated with adherence:**

  Sex: men were less likely than women to have pre-DMF urinalysis, or on-DMF liver or lymphocyte tests.

  People with previous exposure to a non-oral DMT were more likely to be monitored for pre-treatment liver and lymphocyte tests.

  All other patient characteristics including age, socioeconomic status, and comorbidity were not significantly associated with adherence to laboratory testing pre-treatment or on-treatment.

Conclusions

- Adherence to recommended laboratory testing was high (>77%) before oral DMT initiation, but lower once on drug.
- There is a need to understand the long-term consequences of suboptimal laboratory monitoring in the DMT-treated MS population.
- The sex differences warrant further investigation.

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