DIMETHYL FUMARATE REDUCES FATIGUE IN PATIENTS WITH RELAPSING REMITTING MULTIPLE SCLEROSIS - A PROSPECTIVE 2 YEAR PHASE IV TRIAL





Louise Andersen MD¹, Zsolt Illés MD, PhD^{1,2,3}, Tobias Sejbaek MD, PhD^{1,2,3,4}.

¹ Department of Clinical Research, University of Southern Denmark, BRIDGE, Odense, Denmark. ² Department of Neurology, Odense University Hospital, Odense, Denmark. ³ MS Alliance of Southern Denmark, Denmark.⁴ Department of Neurology, Hospital of South West Jutland, Esbjerg, Denmark.

INTRODUCTION & OBJECTIVES

MS Fatigue is the most frequent symptom affecting 65%-90% of MS patients, and is also reported as one of the most disabling symptoms impacting QoL more than physical aspects of MS, e.g. spasticity. However, the pathophysiology, and thereby treatment, of fatigue still remains uncertain. Dimethyl fumarate (DMF) is a recent oral DMT against relapsing remitting multiple sclerosis (RRMS)



which is both anti-inflammatory and neuroprotective. However, no

study has investigated changes of fatigue during treatment with DMF. To investigate fatigue in patients with relapsing remitting multiple sclerosis (RRMS) before and after treatment with DMF.

METHODS

Prospective phase IV trial with 52 newly diagnosed treatment naïve patients with RRMS. Fatigue was evaluated with Fatigue Scale of Motor and Cognitive Function (FSMC) and the Modified Fatigue Impact Scale (MFIS) at baseline (BL) after 3, 6, 12 and 24 months (given as lowered numbers after fatigue scales). We use Kruskal Wallis multiple comparison, Spearman linear regression, standard deviation given in brackets.



Month

Month

Figure 1. The Modified Fatigue Impact Scale (MFIS) mean score in total and in physical, cognitive and psychosocial subscores at baseline, 3, 6, 12 and 24months illustrated with error bars (Standard Error of the Mean). Significant mean decrease marked with * (p<0.05) and ** (p<0.01)



Patients KKIVIS	Female	Age (± SD)	ED22 (± 2D)
N = 52	42 (80.8%)	33 ± 8.04	1.73 ± 0.91

Table 1. Baseline Demograpichs. Gender, Age and Expanded Disability Status Scale (EDSS) ± Standard Deviation at the time of inclusion.

RESULTS

- Patients were on average fatigued with following baseline values: MFIS_{BI} of 31.2(\pm 20.4) and FSMC_{BI} of 46.7 (\pm 20.8).
- MFIS scores demonstrated a significant reduction after treatment with DMF at;
 - MFIS₃: 7.85 (\pm 12.20; p=0.003**) $MFIS_6$: 7.75 (±15.59; p=0.0032**) MFIS₁₂: 8.40 (±15.55; p=0.0015**) MFIS₂₄: 10.25 (\pm 10.92; p=0.000**)

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	0	3	6	12	24	18	0	3	6	12	24	-	18	0	3	6	12	24
Month					l	Mont	h					I	Mont	h				

Figure 2. The Fatigue Scale for Motor and Cognitive functions (FSMC) – the total score, motor and cognitive subscores at baseline and month 3, 6, 12 and 24 are shown with error bars (Standard Error of the Mean). Significant mean decrease marked with * (p<0.05)

Changes in Motor, Cognitive and Psychosocial subscales of Fatigue – *MFIS & FSMC*

	Baseline	3months	6months	12months	24months
IFIS COGNITIVE	15.28(±10.83)	12.33(±9.06)**	12.40(±9.26)*	12.30(±10.10)*	12.31(±9.79)**
IFIS PHYSICAL	14.95(±9.51)	10.74(±7.97)**	10.80(±7.96)**	10.15(±7.92)**	9.94(±6.33)**
IFIS psychosocial	2.23(±2.19)	1.54(±1.73)**	1.42(±1.74)*	1.27(±1.81)**	1.66(±2.06)*

FSMCCOGNITIVE 21.48(±11.65) $22.96(\pm 10.46)$ $21.55(\pm 10.54)$ $21.22(\pm 10.19)$ $21.76(\pm 10.72)$ **FSMC**MOTOR $23.78(\pm 10.85)$ $21.61(\pm 9.97)^*$ $21.27(\pm 9.71)^*$ 20.98(±9.47)* 21.88(±11.28)

Mean values with Standard Deviation. Significant mean decrease, p<0.05 * p<0.01**



FSMC scores were <u>decreased</u> at follow-up: FSMC₃ of 3.25 $(\pm 12.07; p=0.096), FSMC_6: 3.42 (\pm 13.17; p=0.096), FSMC_{12}: 3.67$ $(\pm 15.73; p=0.133)$ and FSMC₂₄: 3.87 $(\pm 13.51; p=0.121)$, however not significant.

- Self-reported health perception correlated with levels of fatigue and subscales for motor and cognition:
 - MFIS (r=0.52, $p<0.01^*$) and FSMC (r=0.53, $p<0.01^*$).
- Self-reported health perception correlated with Beck's **Depression Inventory Fast Screen**
 - BDI-FS (r = 0.0474, p<0.01*)

MS fatigue improved significant after 3 months of treatment with DMF and reduction was sustained during treatment at up to 24months follow-up when measured by MFIS. FSMC showed a similar trend but results were, however, not significant. Selfreported outcomes are affected by mood and general health perception.

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