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ORIGINAL ARTICLE

Pilot study of longterm low fat diet in relapsing-remitting multiple sclerosis

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Abstract

BACKGROUND AND OBJECTIVE: To assess longterm feasibility of low saturated fat diet (less than 15 g of saturated fat per day) in patients with relapsing remitting multiple sclerosis (RRMS) and its effect on the course of the disease.
MATERIALS AND METHODS: Patients were enrolled into a single arm, prospective study. The eligibility criteria included the diagnosis of RRMS according to the McDonald criteria 2010 and the ability to comply with the diet. Patients were allowed to receive disease modifying therapy (DMT) and to take food supplements. Diet adherence was monitored by food diaries. Number of attacks, brain magnetic resonance imaging (MRI) characteristics, Expanded disability status scale (EDSS) and Body mass index (BMI) were recorded.
RESULTS: Twelve patients with RRMS were enrolled. Six patients (50%) continued with the diet for the median duration of 37 months. The high drop-out of patients was caused mainly by patients' inability to strictly adhere to the diet. In six patients who were able to follow the diet – their mean EDSS of 1.30 decreased to 1.17. None of the patients experienced an attack, 5 of 6 patients had stable disease on yearly magnetic resonance imaging (MRI) scans with no new lesions identified.
CONCLUSION: The low fat diet is safe and seems to be effective in preventing clinical attacks/new MRI lesions. The main drawback is the problem of adhering to the diet longterm in the western-style diet environment.

Abbreviations:

MS	- Multiple sclerosis
RRMS	- Relapsing– remitting multiple sclerosis
DMT	- Disease modifying therapy
EDSS	- Expanded disability status scale
BMI	- Body mass index
MRI	- Magnetic resonance imaging
T2/Flair	- T2 weighted/fluid attenuated inversion recovery
EAE	- Experimental autoimmune encephalomyelitis
OMS diet	- Overcoming multiple sclerosis diet
CSF	- Cerebrospinal fluid
NEDA 3	- No evidence of disease activity 3

INTRODUCTION

Diet is being increasingly recognised as a modifiable risk factor for multiple sclerosis (MS) disease progression, a recent study provides epidemiologic association between dietary habits and level of sustained disability. (Fitzgerald at al. 2018) Evidence suggests that various factors in diet composition can enhance or diminish inflammation and that dietary fats are an important factor. In addition to the amount of fat, the types of fats consumed can have a major impact on human health. (Fritsche, 2015) The exposure of inflammatory cells to different types of fatty acids can influence their function and modify inflammatory processes. They act directly via 'fatty acid receptors´ and so have an effect on gene expression or act as precursors of extracellular signaling molecules such as prostaglandins (Calder, 2012). Another mechanism connecting diet with immunopathology is the composition of human gut microbiota. Different types of microorganisms have pro- or anti-inflammatory effects on gut lymphoid tissue. Studies indicate that dietary fats greatly influence the gut microbiota composition as well as the course of experimental autoimmune encephalomyelitis (EAE), the laboratory mouse model of MS (Van den Hoogen *et al.* 2017). Several independent investigations have demonstrated mitochondrial respiratory chain deficiency in MS, as well as abnormalities in mitochondrial transport, linking energy metabolism with neurodegeneration and neuroinflammation. (Barcelos et at. 2019) Several diets have been popularized within the MS community, but the best evidence for efficacy so far exists for the low saturated fat diet published by Swank (Swank & Dugan, 1990) and its derivative, the Overcoming Multiple Sclerosis diet (OMS diet), made popular by Jelinek (Jelinek, 2016). Research has also shown that following OMS and Swank diet program was associated with higher overall diet quality (Simpson-Yap *et al.* 2021). Apart from the study by Yadav (Yadav *et al.* 2016) who followed patients on low fat diet for 1 year and failed to show a clear benefit on disease progression, there are no other published patient cohorts describing the longterm effect of this diet. There are case studies published in non-scientific literature (Jelinek & Law, 2013), which keep on inspiring a number of MS patients.

Our aim was to follow up patients comitted to adhere to low saturated fat diet longterm, to assess its tolerability and feasability in real life and its effect on EDSS, relapse rate and MRI lesion load.

MATERIALS AND METHODS

Subject recruitment

Patients were enrolled from 09/2016 to 09/2020 into a single arm, prospective study. The information about the study was distributed to patients via biannual talks organised by the Slovak Multiple Sclerosis Society for a wider patient audience from 2016 to 2019 as well as via the MS Society magazine. The eligibility criteria were the diagnosis of RRMS according to the McDonald criteria 2010 (Polman *et al.* 2011), at least 1 relaps in the preceding 2 years and the ability to comply with the diet and study protocol. Patients were allowed to receive DMT and to take food supplements.

Study approval

The study was approved by the Ethics committee of Faculty Hospital in Nitra, Slovakia, and all subjects provided informed consent.

Study procedures

At the first visit, demographic information – age, sex, education, smoking habit – were recorded. MS-related data included age at diagnosis, disease duration, history of relapses, past/current disease-modifying therapies, cerebrospinal fluid (CSF) oligoclonal band status, past/current diet modifications, vitamin and food supplements.

Diet intervention

Interested subjects were provided detailed information on the longterm nature of their life-style/diet change and the need for follow up. Although the diet restriction was limited to a single modality – saturated fat, the amount of which should not exceed 15 g per day,

Tab. 1. Baseline characteristics (n=6)

Patient	Sex	Age at disease onset	MS duration (years)	Type of MS	Initial EDSS	Education*	BMI
JV	F	38	7	RRMS	1.5	3	19
LO	F	34	0.5	RRMS	1	3	20
NB	F	28	0.5	RRMS	1	3	21
HH	F	37	8	RRMS	1	3	20
KSO	F	35	2	RRMS	2	3	23
LŠ	F	31	1.5	RRMS	1.5	3	23

F – female, MS – multiple sclerosis, RRMS – relapsing-remitting multiple sclerosis, EDSS - Expanded disability status scale, BMI – Body mass index, *1 basic, 2college, 3 university degree

the patients were educated on the need to supplement saturated fats by mono- and polyunsarurated fats as suggested by Swank and to follow the Swank protocol (Swank & Dugan, 1987), alternatively patients followed the OMS diet by Jelinek (Jelinek, 2016) – the low saturated fat diet without diary and meat with the exception of fish. The commited patients were provided 2 hour session by the leading investigator to learn how to assess the amount of saturated fat in the diet, received a written information about the diet and the saturated fat contents of various foods as well as link to the web based food content calculator (kaloricketabulky.sk). They were also able to contact the investigator at any time for support by e-mail.

Participants´diet adherence was monitored by food diaries, patients calculated and recorded their daily saturated fat intake and provided a 7 day food diary each month for the first 6 months, then 3 monthly and 6 monthly from the second year on the diet. Diet adherence was also checked during clinic visits.

Clinical outcome measures

At the baseline and each following visit, neurological examination was performed by the investigator, the number of clinical attacks and EDSS was recorded. The visits were scheduled at 1 yearly interval (+/- 3 months), in 2020 there were missing visits caused by COVID 19 pandemic travel restrictions, visits resumed fully in 2021.

MRI

Brain MRI scans 1,5 Tesla with contrast were performed at yearly intervals at patients´ respective MS centres and the number of T2-weighted/Fluid Attenuated Inversion Recovery (T2/Flair) hyperintensities were reported by different certified radiologists.

Tab. 2. Disese activity prior to diet intervention

Patient	Number of relapses (in the last 2 years)	Baseline MRI lesion load
JV	4 (1)	Supratent. 6-7 Infratent. 1 Spinal: yes
LO	2 (2)	Supratent.> 10 Infratent. 1 Spinal: yes
NB	2 (2)	Supratent. >25 Infratent. 4 Spinal: yes
HH	4 (1)	Supratent. 21 Infratent. 1 Spinal: 1
KSO	6 (6)	Supratent. 6 Infratent. 1 Spinal: yes
LŠ	1 (1)	Supratent. >40 Infratent. 1 Spinal: yes

MRI – magnetic resonance imaging, Supratent. – supratentorial, Infratent. – infratentorial

Tab. 3. Disease Modifying Therapy (DMT) during the study

Patient	DMT
JV	glatiramer acetate / dimethyl fumarate
LO	glatiramer acetate
NB	Fingolimod
HH	no treatment
KSO	dimethyl fumarate
LŠ	no treatment

RESULTS

Patients enrollment

Most of the eligible patients interested in life-style change and dietary modification declined participation in the study, most of them considered the longterm diet adherence and follow up commitment to be a potential problem.

From december 2016 to september 2020 only 12 patients were enrolled and 6 (50%) were capable to continue with the diet intervention and follow up commitments longterm. The six patients who did not continue with the diet stopped participating within the first 6 months, 4 could not comply with the diet and completion of diaries, one patient got pregnant and stopped the diet and 1 patient claimed raised liver function tests to be the reason for stopping.

Patients demographics

Baseline patient demografics are in table 1, 2 and 3. Average age was 33,8±3,8 years at study entrance, average duration of illness 3,3+/-3,4 years and the subjects had relatively low initial EDSS (1,3+/-0,4). They all had RRMS with relatively high lesion load on MRI scans and at least 1 relaps during preceding 2 years. They were all non-smokers, with normal BMI and all had university education.

Clinical outcomes

Number of relapses, change in EDSS and number of new lesions on brain MRI are summarized in table 4. The study participants able to adhere to the low fat diet longterm were all highly motivated young women who considered the diet change a lifelong commitment and their diet compliance was excellent. They adhered to the diet containing less than 15 g of saturated fat daily for 90–100% of the time.

One subject (JV) reported sensory symptoms considered a possible clinical relapse, she was also given a couse of high dose steroids on outpatiet basis and her DMT was changed from glatiramer acetate to dimethyl fumarate. However, after obtaining a thorough history and repeat imaging of the brain and whole spinal cord

Tab. 4. Duration of diet, number of relapses, change in EDSS and number of new lesions on brain MRI

Patient	Duration of diet (months)	Number of relapses on diet	Change in EDSS	New lesions on MRI
JV	54	0	0	0
LO	48	0	0	0
NB	37	0	0	0
HH	54	0	0	2
KSO	18	0	-0.5	0
LŠ	15	0	0	0

EDSS - Expanded disability status scale, MRI – magnetic resonance imaging

(which showed no new or enlarging lesions), these symptoms were considered unlikely to represent an MS relapse.

Five out of 6 patients (83%) reached No Evidence of Disease Activity 3 (NEDA 3) status during the follow up so far (average follow up duration was 37 months). This might be considered favorable compared with published data on NEDA 3 achievability (Rotstein *et al.* 2015, Parks *et al.* 2018). In our cohort, the most potent drug taken by 1 patient was fingolimod, other patients had less potent medications or no DMT. In published study (Radue *et al.* 2012) – 50.7% of patient receiving fingolimod over the period of 24 months achieved NEDA 3 compared with 21% of patients on placebo, however, the mean EDSS and disease activity in the cohort was higher than in our sample.

DISCUSSION

The significance of diet and its effect on disease progression in multiple sclerosis has been investigated for more than 70 years. Epidemiological (Lauer 1994, Esparza *et al.* 1995, Ghadirian *et al.* 1998) as well as case control studies (Hadgkiss *et al.* 2015, Azary *et al.* 2017, Fitzgerald *et al.* 2018) are providing evidence on an important role of diet in development and progression of MS. Diet with a higher content of animal products is generally considered pro-inflammatory, diet with a higher proportion of fruits and vegetables is thought to have an anti-inflammatory effect. Apart from antioxidants, poly- and monosaturated fats have anti-inflammatory properties, whereas saturated fats increase inflammation (Shivappa *et al.* 2014). It is impossible to perform a controlled, randomized, double blind study in a longterm diet intervention in humans, diet is a complex issue and it is hard to prove the effect of a single diet ingredient on disease progression. Professor Swank followed a sample of 144 MS patients on low saturated fat diet for 34 years and his results, showing the diet being extremely beneficial in stopping disease progression, are very likely not appreciated enough. The only randomized study following 32 MS patients on purely vegan low saturated fat diet for 12 months did not show any effect on disease progression (Yadav *et al.* 2016). However, patients both in the intervention and control group were randomized from a cohort of patients interested in this type of diet. There are to our knowledge no futher cohorts of patients commited to Swank diet reported in the literature.

The main limitation of this pilot study is the small number of patients. We found that to enroll participants to a study where a significant diet commitment for a long period of time is necessary is, as could be expected, not easy. In the 1950-ies when Prof. Swank enrolled his patients, the diet intervention might have been the only treatment offered with much higher patient enrollment success. 50% of patients in his cohort were capable to follow the diet strictly. (Swank & Dugan, 1990) To adhere to a diet restriction longterm is possible if the patient is highly motivated and convinced of the beneficial effect of this diet intervention on MS. This was also shown in a recent study by Katz Sand, where patients were able to adhere to Mediterranean diet (Katz Sand *et al.* 2019). Patients also appreciate that the diet works in preventing cardiovascular and neurodegenerative diseases as well as cancer and has no side effects. The analysis of micronutrient content in Swank diet shows it to be nutritionally more valuable compared with common diet (Titcomb *et al.* 2021). Although the sample of patients described in the study is small, the trend towards disease stability and little clinical as well as imaging disease progression was demonstrated. Futher studies are needed.

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Declaration of Competing Interests

The authors declare that they have no conflict of interest.

Consent for publication

All authors revised and approved the final version of the manuscript.

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