Ketogenic diet and prolonged fasting improve health-related quality of life and lipid profiles in multiple sclerosis – A randomized controlled trial

Markus Bock MD[1,2,3]; Andreas Michalsen MD[4]; Friedemann Paul MD[1,2]

[1]Experimental and Clinical Research Center, a joint cooperation between the Charité Medical Faculty and the Max-Delbrück Center for Molecular Medicine, Berlin, Berlin, Germany.

[2]NeuroCure Clinical Research Center and Clinical and Experimental Multiple Sclerosis Research Center, Department of Neurology, Charité University Medicine Berlin, Berlin, Germany.

[3]Integrative Proteomics and Metabolomics, Berlin Institute of Health (BIH), Berlin, Berlin, Germany

[4]Institute of Social Medicine, Epidemiology and Health Economics, Charité University Medicine Berlin, Berlin, Germany.

Background

Ketone bodies may mediate neuroprotection. Ketone oxidation is compensated by equal reduction in glucose oxidation in the brain under prolonged fasting (PF) or ketogenic diet (KD) conditions. KD and prolonged effectively fasting modulate the immune system in experimental autoimmune encephalomyelitis. We show that PF or KD ameliorate health-related quality of life (QOL) measures in relapsing remitting multiple sclerosis (RRMS).

Hypothesis

KD and PF improve the Multiple Sclerosis Quality of Life-54 (MS-54) scale in RRMS patients.

Methods

RCT and parallel-group 6-month pilot study after ethical committee approval (NCT 01538355). 60 RRMS patients were recruited from July 2011 to August 2012. The patients received disease modifying therapy or no immunomodulatory treatment. Ketonuria-/aemia was monitored. One group received a usual diet, another group enhanced their diet with an initial 7-day fasting episode. A third group received KD from the outset. We used MS-54 self-assessment questionnaires and measured the blood lipid profiles.

Results

Tab. 1 Patients baseline characteristics

	Total (n=48)	SD IQR	Control (n=12)	SD IQR	Fasting (n=18)	SD IQR	Ketogenic (n=18)	SD IQR	*p-value
Age in years	44.8	10.4	50.5	10.4	44.4	11.1	41.3	8.2	*ns*
Gender F/M	38/10 (79/21)		9/3 (75/25)		15/3 (83/17)		14/4 (78/22)		*ns*
Expanded disability status score	3.0	2,0-4	2.5	1,5-4	4.0	2,4-4	3.0	2,4-3,5	*ns*
Disease Duration in years	8.9	7.3	9.9	9.2	11.0	7.7	6.3	4.3	*ns*
Relapse rate 12 months prior study outset	0.4	0.5	0.3	0.7	0.4	0.5	0.4	0.5	*ns*
No immunomodulatory treatment	11 (23)		3 (35)		2 (11)		6 (33)		*ns*
Glatirameracetate	15 (31)		7 (58)		6 (33)		2 (11)		**<0.05**
Interferon beta 1a	9 (19)		1 (8)		6 (33)		2 (11)		*ns*
Interferon beta 1b	3 (6)		0.0		1 (6)		2 (11)		*ns*
Fingolimod	4 (8)		0.0		1 (6)		3 (17)		*ns*
Natalizumab	4 (8)		1 (8)		1 (6)		2 (11)		*ns*
Intravenous immuneglobulin	2 (4)		0.0		1 (6)		1 (6)		*ns*
BMI	26.7	5.5	27.3	6.9	26.0	4.8	26.9	5.3	*ns*
Percent Body Fat	36.6	10.4	38.0	10.6	35.7	9.9	36.5	11.3	*ns*
Physical Health Composite; (n=12,13,13)	67.4	15.2	73.1	8.8	59.6	15.6	69.9	15.2	*ns*
Mental Health Composite; (n=12,17,15)	71.1	16.8	75.4	13.6	64.2	19.1	75.5	14.7	*ns*
Total Cholesterol, mg/dl	203.5	32.1	220.8	28.7	209.7	27.0	198.6	41.4	*ns*
*L*ow *D*ensity *L*ipoprotein, mg/dl	124.3	32.1	129.8	31.1	126.3	25.5	119.7	36.7	*ns*
*H*igh *D*ensity *L*ipoprotein, mg/dl	68.1	17.8	69.9	17.1	62.9	17.9	62.1	18.1	*ns*
LDL/*HDL* ratio	2.0	0.8	2.0	0.9	2.2	0.8	2.1	0.8	*ns*
Triglycerides, mg/dl	89.3	42.9	105.1	43.2	111.1	48.2	87.2	36.4	*ns*

Data are mean ± SD, or median with inter quartile range or number (percent); baseline data were available for 48 patients deviations are given in brackets; *Kruskal Wallis test for comparison between the three groups was performed.

Fig. 1 Representative baseline values on MS-54

Comparison of the mean MS-54 scores of patients from the present study to US MS patients[1]. *Abbreviations:* PHCS= physical health composite, MHCS= mental health composite, SXF= sexual function, HD= health distress, OQL= overall quality of life, CF=cognitive function, *PF=physical function, HP= health perception, E/F= energy / fatigue, RP= role limitations physical, P= bodily pain, SoF= social function, EW= emotional well-being. RE= role l*imitations emotional. [1] Vickrey et al. (1995)

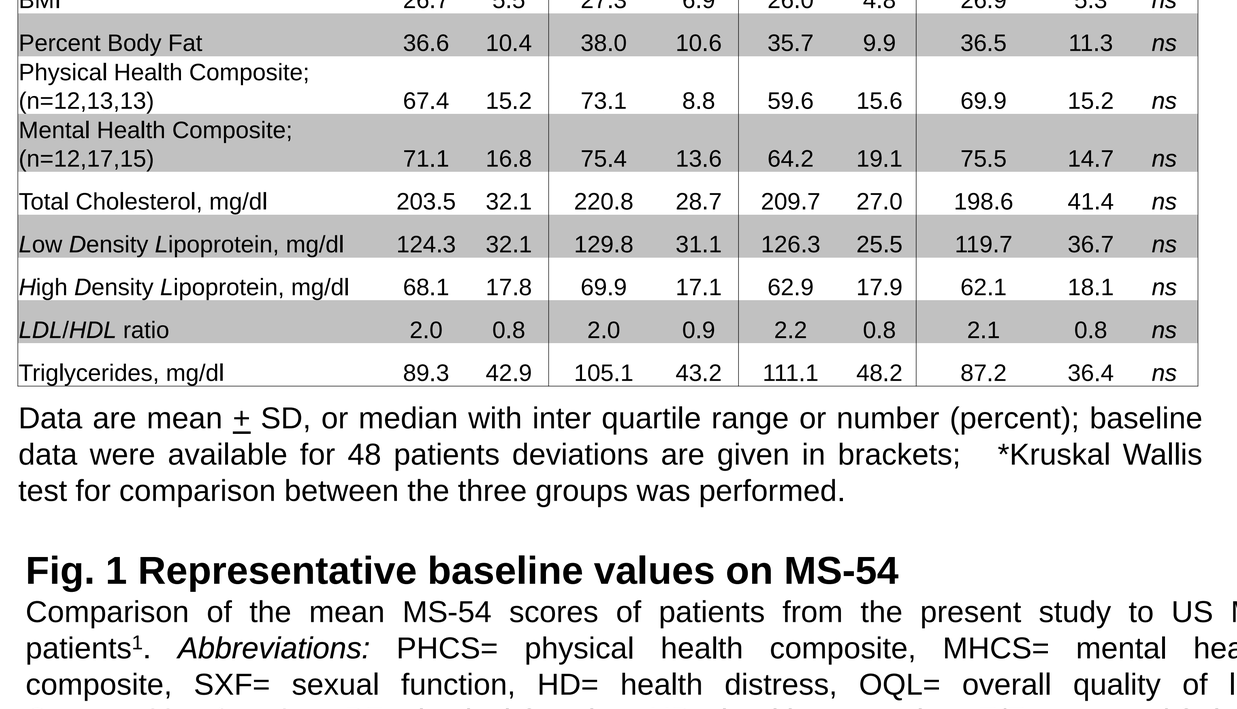

Fig. 2 a-d Longitudinal MS-54 changes

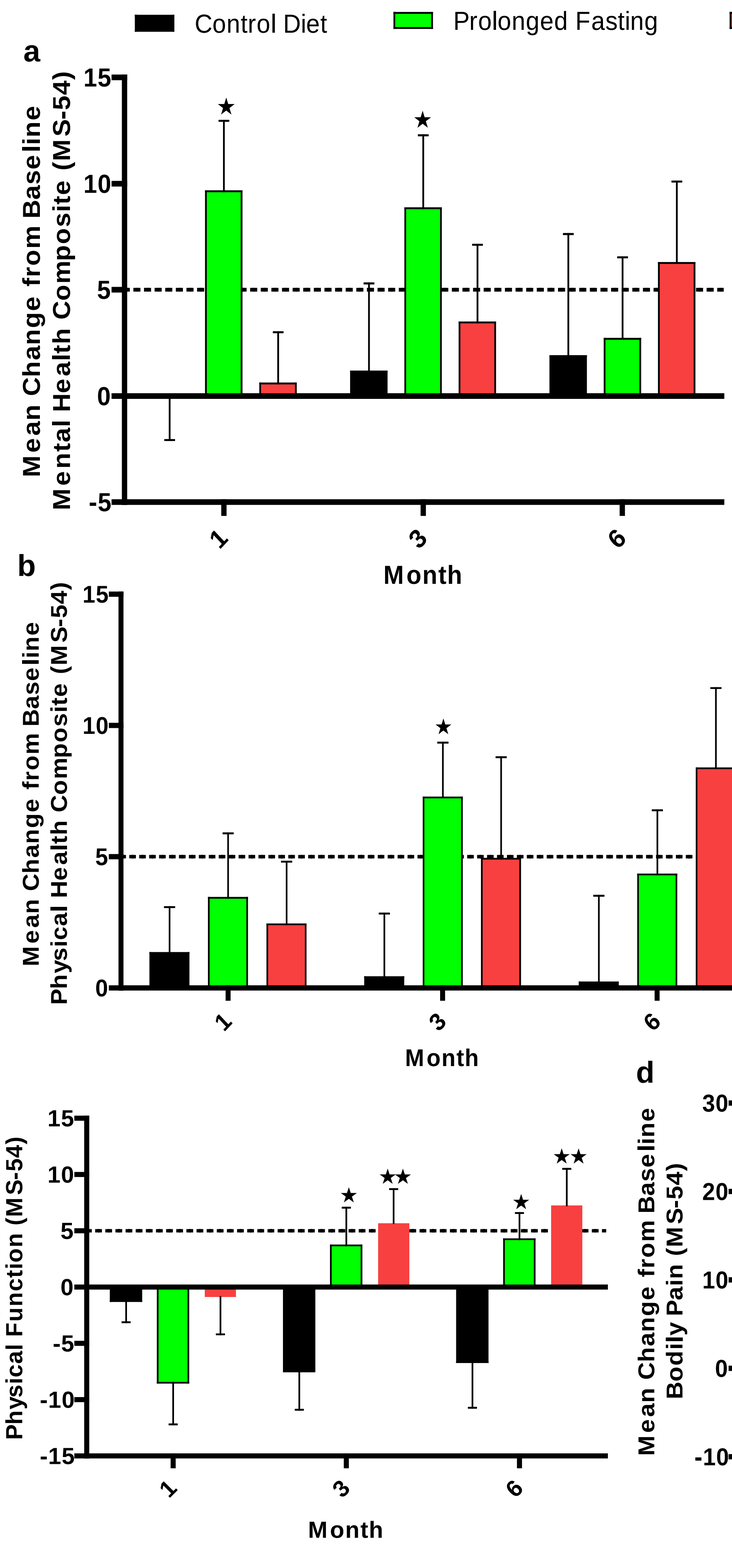

Fig. 2 a-d
PF and KD improve summary (a+b) and single (b+c) MS-54 scores in MS Patients. MS-54 data are mean+SEM. Dotted line represents threshold which is thought to be a clinically meaningful gain (≥5 points) in MS-54 outcome. *p<0.05, **<0.01 Mann-Whitney-U test was performed to compare the mean change from baseline between the control group and the PF or KD groups. In PF a maximum effect size was found at month 3 (0.8) and in KD at month 6 (0.7).

Fig. 3 a+b Longitudinal blood lipid changes

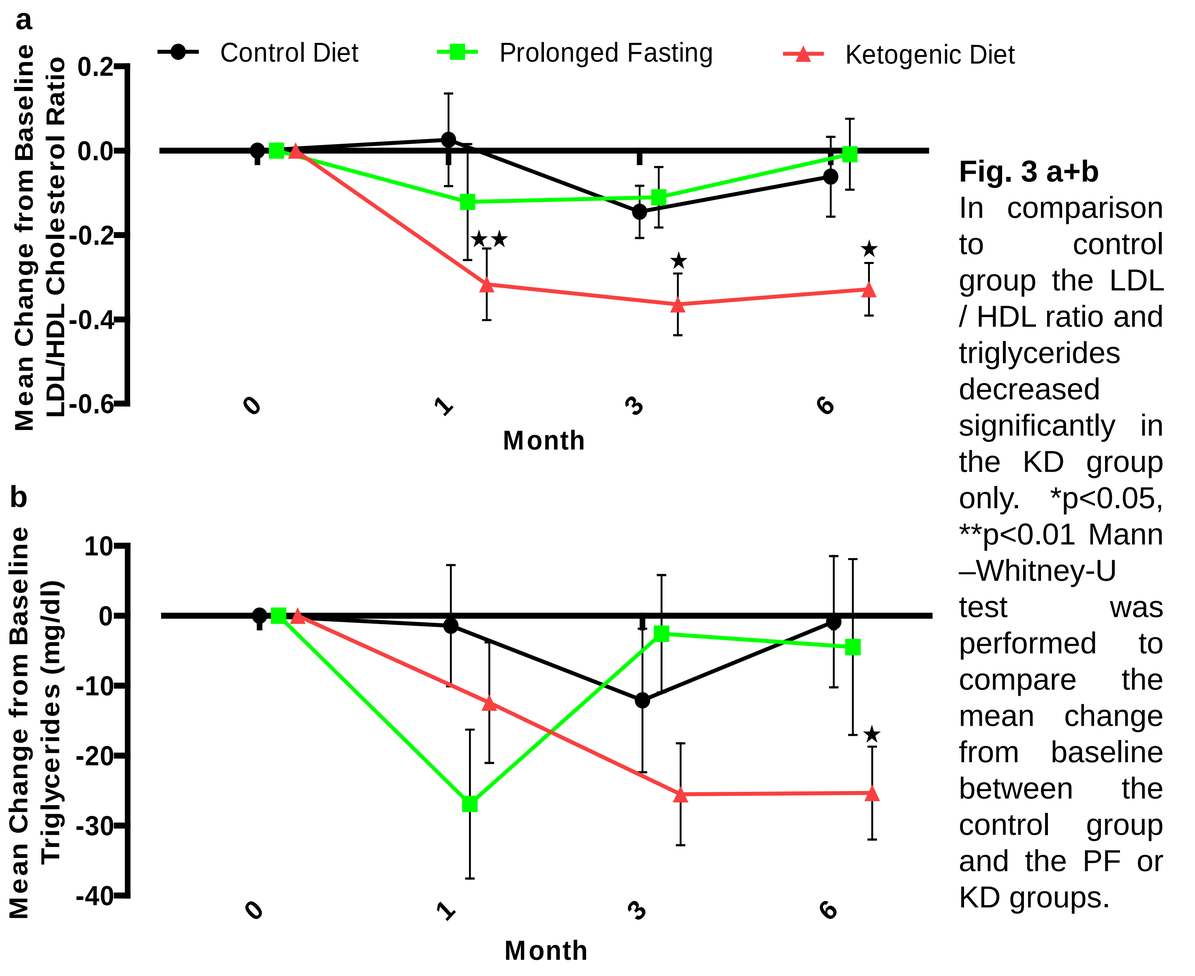

Fig. 3 a+b
In comparison to control group the LDL / HDL ratio and triglycerides decreased significantly in the KD group only. *p<0.05, **p<0.01 Mann –Whitney-U test was performed to compare the mean change from baseline between the control group and the PF or KD groups.

Conclusions

PF and KD are feasible in RRMS patients. QOL and lipid profile improve with KD and PF. KD has a sustainable, specific effect on LDL/HDL ratio and triglycerides, which may be associated with disease progression. KD and PF could favorably influence RRMS outcomes when coupled with conventional treatments.

Corresponding Author: markus.bock@charite.de