REGION VÄSTRA GÖTALAND
SAHLGRENSKA UNIVERSITY HOSPITAL

DEPARTMENT OF PEDIATRICS

UNIVERSITY OF GOTHENBURG

Prospective study of growth in Swedish children treated with modified ketogenic diet

Anna Svedlund[1], Tove Hallböök[1], Per Magnusson[2], Jovanna Dahlgren[1], Diana Swolin-Eide[1]

[1]Department of Pediatrics, The Queen Silvia Children's Hospital, Institution of Clinical Sciences, Sahlgrenska Academy at University of Gothenburg, Sweden, [2]Department of Clinical Chemistry, Linköping University, Sweden

Purpose

Modified ketogenic diet (MKD) is one treatment option for intractable epilepsy and metabolic conditions such as glucose transporter type 1 deficiency syndrome (GLUT1-DS) and pyruvate dehydrogenase complex (PDC) deficiency.

MKD is a less restrictive diet than the classical ketogenic diet (KD) and thus more tolerable and, moreover, some studies indicate that prolonged KD treatment can negatively affect linear growth in children. Long-term data is missing regarding the effects of MKD treatment in children.

This study was designed to prospectively assess growth in children treated with MKD for 24 months.

Patients with intractable epilepsy

Gender	Age at start of MKD	Etiology	Epilepsy syndrome	Physical status	3-hydroxybutyric acid 0/6/12/24 months	Lactate 0/6/12/24 months	Seizures per month 0/6/12/24 months
M	3.8	Unknown	Lennox Gastaut	A	<0.1/1.4/2.3/1.1	1.7/1.1/1.4/–	200/8/8/8
F	14.8	Encephalitis	-	A	<0.1/2.6/1.0/–	0.9/1.0/0.9/–	15/3/3/–
F	3.6	Mitochondriopathy	-	NA	<0.1/4.7/3.8/3.6	0.6/0.6/1.0/–	200/20/20/10
M	2.3	Cortical malformation	Lennox gastaut	NA	<0.1/2.2/1.4/3.6	2.4/–/1.1/0.9	500/300/300/300
F	16.3	Cortical malformation	Lennox Gastaut	A	<0.1/–/–/–	1.5/1.1/–/–	240/240/–/–
M	4.0	Genetic epilepsy	Doose	A	<0.1/3.0/2.8/2.1	1.9/1.1/1.0/1.6	200/0/0/0
M	8.5	Encephalitis	Lennox Gastaut	NA	0.2/3.4/2.3/2.7	1.2/1.1/1.2/1.0	340/340/340/340
M	2.3	Stroke	West Syndrome	NA	0.21/2.8/–/–	1.2/1.3/–/–	400/280/–/–
M	4.5	Mitochondriopathy	-	NA	0.1/2.3/1.9/2.1	0.9/0.8/0.9/1.2	150/100/75/75
M	5.7	Unknown	Lennox Gastaut	NA	<0.1/1.8/–/–	1.7/0.8/1.6/0.7	400/250/250/250
M	1.6	Unknown	West syndrome	NA	<0.1/2.3/1.4/–	1.5/4.1/1.6/-	180/180/180/–
M	2.3	Genetic epilepsy	West syndrome	NA	0.7/2.3/4.9/–	0.5/1.1/1.1/2.0	500/300/300/300
F	6.2	Genetic epilepsy	Doose	A	0.2/2.9/3.2/–	1.3/1.3/1.3/–	150/25/25/–
F	3.8	Genetic epilepsy	Dravet	A	<0.1/2.5/0.2/–	1.3/1.2/1.3/–	300/200/200/100
M	8.7	Cortical malformation	Lennox Gastaut	NA	0.13/2.3/–/–	1.1/1.4/–/–	500/500/–/–
F	3.0	Genetic epilepsy	Doose	A	<0.1/2.3/3.8/3.3	1.8/1.1/–/1.5	300/0/0/0
M	5.4	Unknown	Lennox Gastaut	NA	0.2/3.8/3.4/2.9	0.7/0.8/1.3/0.8	1090/280/280/280
F	10.0	Tuberous Sclerosis	Lennox Gastaut	A	0.3/5.2/3.8/4.8	1.5/–/1.9/0.9	1532/50/50/50
F	3.7	Stroke	Lennox Gastaut	NA	0.11/2.4/–/–	1.5/1.3/–/–	230/250/–/–
M	15.0	Genetic epilepsy	Doose	A	–/4.2/2.8/3.4	1.1/1.1/1.2/1.1	330/6/6/6
M	5.5	Tuberous Sclerosis	Lennox Gastaut	A	<0.1/3.4/2.0/2.4	1.2/1.3/1.4/1.4	60/10/10/10
F	4.8	Aicardi syndrome	Lennox Gastaut	A	0.39/2.6/2.3/2.6	1.2/2.3/1.1/1.0	36/22/22/22

Patients with GLUT1-DS

Gender	Age at start of MKD	Epilepsy syndrome	Physical status	3-hydroxybutyric acid 0/6/12/24 months	Lactate 0/6/12/24 months	Seizures per month 0/6/12/24 months
F	17.2	Absence	A	<0.1/1.4/2.3/1.1	1.7/1.1/1.4/–	30/0/0/0
F	13.2	Absence	A	<0.1/1.2/2.7/1.7	1.8/–/1.1/1.1	5/0/0/0
F	3.6	Absence	A	<0.1/1.4/2.1/0.9	1.0/0.7/0.9/1.2	40/0/0/0
F	1.5	–	A	0.2/3.3/2.9/3.7	0.9/1.1/1.1/1.2	0/0/0/0
M	4.2	Absence	A	–/–/–/4.9	–/1.2/0.8/0.9	30/0/0/0
M	16.7	Absence	A	<0.1/3.5/4.2/1.8	1.9/1.0/–/1.2	11/0/0/0
M	0.4	–	A	<0.1/3.0/2.9/3.2	0.8/1.1/1.0/1.1	0/0/0/0

Patients with PDHCD

Gender	Age at start of MKD	Epilepsy syndrome	Physical status	3-hydroxybutyric acid 0/6/12/24 months	Lactate 0/6/12/24 months	Seizures per month 0/6/12/24 months
F	4.2	West syndrome	NA	0.2/0.7/0.3/–	2.4/1.9/1.6/–	90/20/20/–
F	2.6	–	NA → A	–/0.8/0.9/1.2	2.3/1.4/1.6/3.1	0/0/0/0
F	2.0	–	A	0.2/1.4/2.0/3.3	4.0/1.5/1.4/–	0/0/0/0
F	9.5	–	A	<0.1/0.4/0.9/0.2	2.5/1.6/–/2.1	0/0/0/0
M	6.0	–	A	2.2/1.5/–/2.3	1.6/0.9/–/1.7	0/0/0/0
F	6.1	–	A	<0.1/–/2.8/2.3	2.0/1.9/1.5/1.5	0/0/0/0
F	8.0	–	A	–/–/–/1.8	0.6/1.1/1.1/1.2	1/0/0/0
F	1.3	West syndrome	NA	<0.1/1.1/1.8/1.6	4.4/0.9/1.1/2.9	150/110/60/60
F	1.1	–	NA	<0.1/2.4/2.9/2.0	3.0/1.5/1.6/1.5	0/0/0/0

Conclusion

- This is the first study to assess the long-term effects on growth in children treated with the MKD.
- No negative effect was observed on longitudinal growth after MKD treatment for 24 months.

Methods

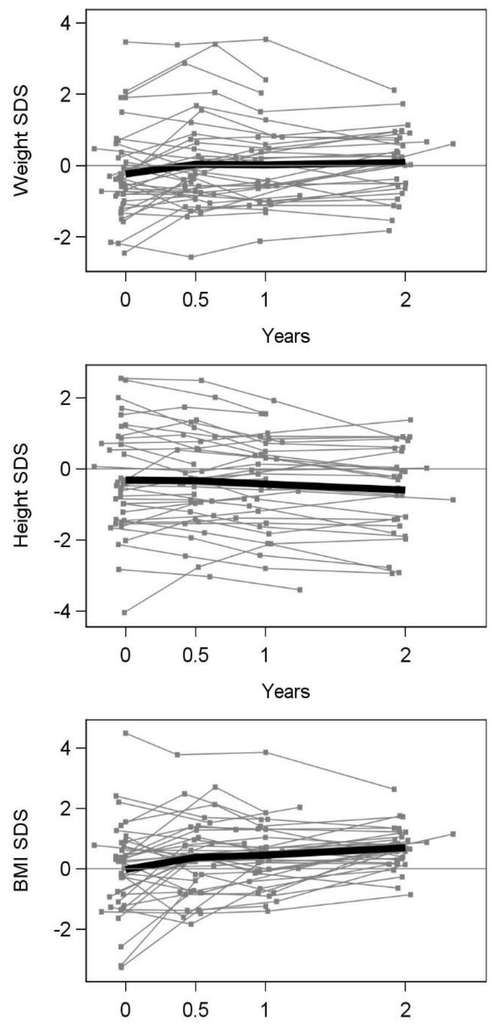
The included patients (n=38; 21 girls, 17 boys) had a mean±SD age of 6.1±4.8 years at MKD initiation. Underlying etiologies were genetic epilepsy (n=6), GLUT1-DS (n=7), PDC deficiency (n=9), cortical malformation (n=3), mitochondriopathy (n=2), tuberous sclerosis complex (n=2), encephalitis (n=2), stroke (n=2), Aicardi syndrome (n=1) and of unknown etiology (n=4). Thirty patients had seizures prior to MKD. Body weight, height and laboratory tests were assessed at baseline, 6, 12 and 24 months.

Results

After 24 months, 29 patients remained on MKD and 57% responded to the diet with >50% seizure reduction.

Weight SDS and height SDS were stable over 24 months (*P*=0.054 and 0.10 respectively), i.e., weight SDS median (min-max) -0.4 (-2.5 to 3.5) at baseline and 0.2 (-1.8 to 2.1) after 24 months; and corresponding values for height SDS -0.4 (-4.0 to 2.5) to -0.3 (-2.9 to 1.4). BMI SDS increased from 0.2 (-3.3 to 4.5) to 0.7 (-0.9 to 2.6) after 24 months, *P*<0.005.

The median plasma 3-hydroxybutyric acid levels increased from 0.05 mmol/L to 2.35 mmol/L (0.42-5.20 mmol/L) after 6 months, *P*<0.0001, but remained stable thereafter, i.e., 2.30 mmol/L (0.18-4.90 mmol/L) after 12 months and 2.30 mmol/L (0.16-4.90 mmol/L) at 24 months. Median pH was 7.38 (7.23-7.51) at baseline and 7.39 (7.34-7.45) after 24 months, *P*=0.45.



At baseline, median IGF-I SDS was -0.15, which decreased to -0.85 after 6 months and to -1.00 at 12 months. From 12 to 24 months IGF-I SDS increased to 0.05. Median IGFBP3 SDS at baseline was 1.00 and was stable after 6 months, then decreased at 12 months to 0.10. From 12 to 24 months IGFBP3 SDS increased to 0.60.

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Growth and syndromes (to include Turner syndrome)

Anna Svedlund

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