

Pilocarpine

Nitric Oxide

Effect of Ketogenic Diet on the Nitric Oxide of Pilocarpine-induced Status Epilepticus

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Backgrounds and Objectives: Despite of enormous clinical and laboratory researches focused on the useful markers in status epilepticus(SE), clinically applicable methods are not yet available. Although ketogenic diet (KD) is an old method of treating epilepsies, its outstanding antiepileptic effect in some epileptic patients needs re-evaluation of this methods. This study was performed to evaluate the effect of KD on the change of nitric oxide(NO) during the SE.

Methods: After the determination of critical EEG stages in the pilocarpine-induced SE model, serum NO levels were measured with Griess reaction. Open cardiac puncture was done immediately after the four different EEG stages of SE in the KD rats and regular diet (RD) rats. Cessation of SE was done with the 10~20 mg/Kg of diazepam i.p. injection in each stages of SE in KD and RD rats.

Results: Pilocarpine-induced SE showed reliable EEG and behavioral patterns in all rats. Also, KD did not affect the SE induced by pilocarpine in terms of the SE induction time and SE severity. Serum NO was consistently higher in KD rats than RD rats in all SE stages.

Conclusions: KD significantly increases NO during the pilocarpine-induced SE. These finding might contribute the neuroprotective effect of KD in the SE.

Key Words: Status epilepticus, Ketogenic diet, Nitric oxide

SE
가 in
(status epilepticus, SE) vitro 가
가 가
Treiman¹ SE 가 .

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가

1861

Reynold⁵ "Epilepsy" 가

SE 가

Guelpa Marie⁶가 20 4

1921

Geyelin⁷ 3 3 4

가 Geyelin 가

nitric oxide(NO) neuron - spe

Wilhel⁸ 가

cific enolase (ketonemia) 가

NO Peterman¹⁹

가 가 50%

NO 가 , Helmholtz²⁰ 3 1

가 , pentylenetetrazol NO가 50% 가

가 nitric oxide synthase N - nitro - L -

arginine (L - NNA) 4 1938 pheny-

NO가 5 toin

가 NO 가가 , KD

adenosine 가 ,⁶

NOS

7 NO Penfield Jasper²¹

NOS

7 - nitroimidazole(7 - NI) L - arginine

lithium - pilocarpine KD

8 1990

NO가 9 1990

nNOS mRNA 가 ,¹⁶

NOS 가 pentylenetetrazol 가

가 가

10 가 가²²

가 NO KD가 SE NO 가²²

NO 가 KD

13 NO 가 SE

가 NO 가 NO 가

가 NO 가 KD가

SE

가 NO 가 KD

(ketogenic diet, KD) 가 SE

가 pilocarpine

pentylenetetrazole flurothyl KD RD

NO Griess

가

KD

1.

Galen 가 가 360~380 mg/Kg pilocarpine

SE 6~36 pilocarpine 87 mg/Kg ketamine 13 mg/Kg xylazine 0.52 ml/Kg bregma 2.0 mm, 3.0 mm, 4.0 mm gentamycin 12 analogue CD rom 가 F4 - P4, P4 - P3, P3 - F4, F4 - F3 SE 20 가 30 a. SE SE Pilocarpine SE 가 KD가 NO 3 KD RD 8 - hydroxy 64 butyrate SE SE NO 2 (discrete seizure): 가 가 가 3. KD (TD 96355, Harlan Teklad, U.S.A., Table 1).²² (continuous spiking): / 가 3

SE 가 10 PED(periodic epileptiform discharges): 가 PED 5 PED: PED diazepam 10 mg/Kg i.p. 1 2. 3 Sprague-Dawly Scopolamine 1 mg/Kg 30 360~400 mg/Kg pilocarpine hydrochloride

Table 1. Ketogenic diet for experimental rodents, TD 96355 (Harlan Teklad).

Component	g/kg
Casein	173.3
DL-Methionine	2.6
Shortening (Crisco)	586.4
Corn Oil	86.2
Cellulose	87.97
Vitamin Mix, Teklad (40060)	13.0
Chlorine Bitartrate	2.5
TBHQ (antioxidant)	0.13
Mineral Mix, Ca-P Defic. (TD79055)	20.0
Calcium Phosphate, dibasic CaHPO ₄	19.3
Calcium Carbonate CaCO ₃	8.2
Magnesium Oxide MgO	0.4

* TD96355 100 67.43 15.08 0.54
 ([]:[+]=4.3:1). 6.69 Cal/g 90.66% 9.01%
 0.32%

Site test kit(GDS Diagnostics, U.S.A.)
 -hydroxybutyrate(OHB) KD 21 SE 0.43)mM RD 0.33(±0.07) mM (Table 2). 3
) -OHB 7.28(±
 3. SE nitric oxide
 Nitric oxide RD KD
 4. Nitric oxide (NO) SE 가
 Pilocarpine SE가 (Table 3). SE KD NO
 Griess reaction
 nitrite NO²³
 5. SPSS 10.0 NO (±) Pilocarpine 가 t - test 가 SE SE가 CA1, CA3, KD RD SE , , KD 7.4±3.09 (min), 28.6±7.63 (min), PEDs 3.9±0.83 (hrs), PEDs 7.4±3.09 (hrs) SE 17±5.88 (hrs)
 1. Pilocarpine KD RD SE , , KD
 2. -hydroxybutyrate 3 KD -hydroxybutyrate , , , 가 21 (±

Table 2. Blood -hydroxybutyrate levels in rats treated with ketogenic diet for 21days.

Concentration of -hydroxybutyrate (mM)		p-value
KD*	7.28 ± 0.43	<0.001
RD**	0.33 ± 0.07	

* KD: **RD:

Table 3. Concentration of nitric oxide(NO) according to the EEG stages(µM)

	RD*	KD**	p-value
Discrete	0.042 ± 0.0021	0.054 ± 0.0023	<0.05
Continuous spiking	0.047 ± 0.0031	0.056 ± 0.0026	<0.10
E-PEDs [†]	0.048 ± 0.0018	0.066 ± 0.0032	<0.05
L-PEDs [‡]	0.050 ± 0.0021	0.066 ± 0.0029	<0.05

*RD: **KD:

[†]E-PEDs: early periodic lateralized epileptiform discharges

[‡]L-PEDs: late periodic lateralized epileptiform discharges

KD
medium -
가

RD
Nitric oxide(NO)

가 ,
chain triglyceride(MCT)

NO가 가
KD가 NO

. KD 가
가 ,

KD NO

가 , KD
KD

NO

NO

KD

⁵ NO

²⁹ nitric

KD가 가
pentylenetetrazole(PTZ)
(maximal

oxide synthase(nNOS)
zole(7-NI)

SE

7-nitroinda-

electric shock)

NO

NO가

²⁴

KD 가

KD

²⁵

KD 3
pilocarpine

3

가

가

NO 가

KD
carpine

KD가

NO

SE가

KD가 SE

1.

pilocarpine

KD가

KD가 SE

2. 3

가

KD

3.

pilocarpine

PTZ

KD

nitric oxide (NO)

35

PTZ

가

NO

KD

가

PTZ

REFERENCES

KD가

²⁶

12

3, 6, 9

KD

²⁶ Bough ²⁷

KD가

dopamine beta-hydroxylase (DBH) knock-out
ergic system KD 가 noradre²⁸

KD

가
pilocarpine

KD

KD

SE
pilocarpine

가
SE KD

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