Caregiver Perspective of Benefits and Side Effects of Anti-seizure Medications in CDKL5 Deficiency Disorder from an International Database

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Supplementary Table 1. Likelihood of any seizure-related benefits and worsening and any side effects associated with the use of antiseizure medications in 399 individuals with CDD

		Any benefits	Any worsening	Any side effects
Antiseizure medication	n	%, number of events/n		
Cannabidiol	70	80, 45/56	4, 2/56	13, 9/68
Carbamazepine	84	22, 9/41	5, 2/41	24, 17/72
Clobazam	219	46, 72/156	3, 5/156	50, 102/205
Clonazepam	132	48, 43/89	3, 3/89	38, 47/123
Clorazepate	13	50, 4/8	13, 1/8	17, 2/12
Ethosuximide	22	13, 1/8	0, 0/8	28, 5/18
Felbamate	31	40, 8/20	5, 1/20	33, 10/30
Gabapentin	17	40, 4/10	0, 0/10	6, 1/16
Steroids/ACTH	135	49, 42/86	5, 4/86	65, 84/129
Lacosamide	49	48, 16/33	3, 1/33	35, 16/46
Lamotrigine	135	52, 46/89	7, 6/89	24, 29/122
Levetiracetam	347	39, 90/231	2, 5/231	32, 102/321
Nitrazepam	21	44, 4/9	0, 0/9	28, 5/18
Oxcarbazepine	96	34, 20/59	8, 5/59	20, 18/88
Perampanel	31	62, 16/26	4, 1/26	42, 11/26
Phenobarbital	213	34, 43/127	2, 2/127	52, 103/199
Phenytoin	42	32, 8/25	4, 1/25	37, 13/35
Rufinamide	69	37, 19/52	6, 3/52	34, 21/62
Sulthiame	10	-	-	10, 1/10
Topiramate	264	49, 77/158	6, 9/158	38, 94/249
Sodium valproate	291	53, 102/194	1, 2/194	31, 82/266
Vigabatrin	243	56, 95/170	2, 4/170	37, 81/220
Zonisamide	105	48, 35/73	5, 4/73	31, 31/99

n, number of uses; ACTH, adrenocorticotropic hormone

Supplementary Table 2. Encoded family provided comments on seizure-related benefits and worsening and medication side effects associated with the use of Cannabidiol and Perampanel

Cannabidiol	Number of events
Benefits	
Cognitive improvements	1
Decreased seizure frequency	8
Decreased seizure frequency and severity	3
Decreased seizure severity	4
Decreased seizure severity and spasms	1
General improvement in seizure control	2
Immediate reduction in seizures	1
Improved control of tonic-clonic seizures	1
Improved sleep	1
Major improvement in seizure control	3
More sociable	1
Overall improvement	1
Reduced seizure duration	1
Worsening	
Worsening of seizure	1
More frequency seizure	1
Side effects	
Increased appetite and bowel motions	1
Drowsiness and fatigue	1
Sleepiness and fatigue	5
Vomiting	1
Vomiting and nausea	1
Perampanel	
Benefits	
Decreased seizure frequency	2
Decreased seizure severity	4
General improvement in seizure control	1
Side effects	
Initial drowsiness, fatigue and over-excited	1
Initial fatigue	1
Initial irritability	1
Screaming	1
Sleepiness and fatigue	6
Vomiting	1

Supplementary Table 3. Frequency distribution of antiseizure medications currently used[a], by concurrent usage status, in 379 individuals with CDD

	Polytherapy	Monotherapy
n	1,111	95
Antiseizure medication	n (%)	
Sodium valproate	152 (13.7)	16 (16.8)
Levetiracetam	144 (13.0)	12 (12.6)
Clobazam	130 (11.7)	7 (7.4)
Vigabatrin	124 (11.2)	8 (8.4)
Topiramate	108 (9.7)	14 (14.7)
Lamotrigine	65 (5.9)	9 (9.5)
Clonazepam	58 (5.2)	1 (1.1)
Cannabidiol	57 (5.1)	4 (4.2)
Zonisamide	49 (4.4)	2 (2.1)
Phenobarbital	47 (4.2)	4 (4.2)
Rufinamide	32 (2.9)	4 (4.2)
Lacosamide	25 (2.3)	2 (2.1)
Oxcarbazepine	23 (2.1)	2 (2.1)
Perampanel	21 (1.9)	2 (2.1)
Carbamazepine	18 (1.6)	3 (3.2)
Corticosteroids/ACTH	13 (1.2)	0 (0)
Felbamate	12 (1.1)	2 (2.1)
Nitrazepam	10 (0.9)	0 (0)
Clorazepate	9 (0.8)	1 (1.1)
Gabapentin	5 (0.5)	1 (1.1)
Ethosuximide	4 (0.4)	0 (0)
Phenytoin	4 (0.4)	1 (1.1)
Sulthiame	1 (0.1)	0 (0)

[a] currently used at the time of the baseline and/or the follow-up questionnaire
n, number of uses; ACTH, adrenocorticotropic hormone

Supplementary Table 4. Likelihood of any seizure-related benefits and any side effects associated with selected[a] concurrent antiseizure medications currently used[b] in 379 individuals with CDD

ASM combination				Any benefits	Any side effects		Seizure frequency[c]			
							Sz Free	Mild	Moderate	Severe
1st	2nd	3rd	n	%, number of events/n		n	n (%)			
LEV	TPM		13	75, 6/8	50, 5/10	13	1 (8)	5 (38)	6 (46)	1 (8)
LEV	VGB		13	78, 7/9	46, 6/13	10	0 (0)	2 (20)	4 (40)	4 (40)
VPA	CLB		13	63, 5/8	69, 9/13	12	0 (0)	3 (25)	2 (17)	7 (58)
VPA	VGB		11	75, 6/8	33, 3/9	10	0 (0)	3 (30)	4 (40)	3 (30)
VPA	LTG		7	83, 5/6	75, 3/4	6	0 (0)	2 (33)	3 (50)	1 (17)
LEV	ZNS		7	100, 6/6	71, 5/7	7	0 (0)	3 (43)	3 (43)	1 (14)
VGB	TPM		7	100, 4/4	86, 6/7	7	0 (0)	1 (14)	5 (71)	1 (14)
VPA	LEV		6	100, 5/5	40, 2/5	6	1 (17)	1 (17)	4 (67)	0 (0)
VPA	TPM		6	67, 2/3	40, 2/5	5	0 (0)	2 (40)	3 (60)	0 (0)
VGB	ZNS		6	67, 4/6	0, 0/6	5	0 (0)	2 (40)	2 (40)	1 (20)
CLB	TPM		6	80, 4/5	80, 4/5	6	0 (0)	1 (17)	5 (83)	0 (0)
CLB	ZNS		5	100, 5/5	100, 5/5	5	0 (0)	0 (0)	3 (60)	2 (40)
VPA	CLN		5	33, 1/3	50, 2/4	5	1 (20)	2 (40)	1 (20)	1 (20)
LEV	OXC		4	66, 2/3	25, 1/4	4	0 (0)	3 (75)	1 (25)	0 (0)
LEV	CLB		4	100, 1/1	75, 3/4	4	1 (25)	2 (50)	0 (0)	1 (25)
VGB	CLN		4	100, 2/2	50, 2/4	4	0 (0)	1 (25)	1 (25)	2 (50)
LEV	VPA	VGB	6	75, 3/4	80, 4/5	4	0 (0)	0 (0)	2 (50)	2 (50)
LEV	VPA	CLB	6	100, 4/4	83, 5/6	4	0 (0)	2 (33)	2 (33)	2 (33)

[a] limited to dual or triple therapy used by at least 4 uses; [b] currently used at the time of the baseline and/or the follow-up questionnaire; [c] seizure frequency: Sz Free, seizure-free for at least 2 months; mild, weekly or less; moderate, 1-4 per day; severe, at least 5 per day
n, number of uses; ASM, antiseizure medication; LEV, levetiracetam; TPM, topiramate; VGB, vigabatrin; VPA, sodium valproate; CLB, clobazam; LTG, lamotrigine; ZNS, zonisamide; OXC, oxcarbazepine; CLN, clonazepam