Cannabidiol treatment in intractable paediatric epilepsy – a pre and post treatment video-EEG study

Dr Yeeshu Singh, Ms Sandra Gurr, Ms Kylie Hale, Dr Geoff Wallace, Dr Vishal Kapoor, **Dr Stephen Malone**

Queensland Children's Hospital , Centre for Studies in Rare Developmental Disorders, Brisbane Australia Stephen.Malone@health.qld.gov.au

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Introduction

- There is Increasing evidence of the effectiveness of Cannabidiol (CBD) in epilepsy
- However non-blinded studies in CBD may be affected by the influence of carer perception
- Even 'blinded' studies susceptible to influence if CBD is obvious to patient/carer
- An independent assessment of effect of CBD treatment would be ideal
- Limited evidence of the use of EEG in assessing CBD therapeutic effect in children

Objectives

- **Primary:** Determine if there is improvement in vEEG patterns (seizures and interictal features) in patients with refractory epilepsy between baseline and 3-months post-treatment with add-on CBD (Epidiolex®)
- **Secondary:** Explore Carer reported information on seizure and QOL outcome, clinical data (at 3 months of treatment, and through the treatment course), and correlate to EEG data

Methods

- Children (2-18 yrs) with refractory epilepsy of varied aetiologies on the CBD Compassionate Access Scheme (CAS) at QCH (2017 to 2019)
- Inclusion criteria:
  - Daily seizures for the past six months.
  - >=1 epilepsy-related hospital admit last year
  - Failure of at least 5 ASM's
  - Between 1-4 baseline ASM's at stable doses

Methods

- CBD dosing between 5-25 mg/kg/day
- Regular review of seizure outcome, QOL/Global impression Change (GIC), safety monitoring
- 24-hr Video-EEG (vEEG) was obtained prior to commencement of CBD, and at 3 months.
- Two independent reviewers (YS,SM) reviewed de-identified studies for ictal and interictal features.
- EEG : **interictal features** including Epileptiform and ESES features, and **Ictal -** focal, focal with tonic clonic, spasms, Myoclonic, tonic, Absences, convulsive and non-convulsive Status Epilepticus
- Interictal spike load (spike index) using automatic spike detector (Persyst®)

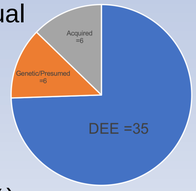
Results

Interictal Analysis : No differences in visual and automated spike analysis

Ictal Analysis: 12186 Seizures (Spasms 4430, Tonic 3644, Myoclonic 1664)

Interrater agreement lowest for tonic (60%), focal (73%), Myoclonic (74%), Spasms (87%)

As a group, **no difference in total EEG seizure count** pre and post CBD studies, including in DS,LGS,Mixed Aetiology group



- **47 patients (F=26) , Av age: 10.3 y**
- **35 patients with DEE**
- **LGS=14, DS=6, Other=27**
- **ASM av 3.4 (CLB=27, VPA=22)**
- **ASM changes through study N=26 CLB reduction N=18**

Variable	Mean (±sd)	Median (IQR)	P value
Total Final Agreed on seizures Pre Post	134 (±202.98) 125.28 (±177.62)	31 (3-178) 50 (2-162)	0.7

Variable	Mean	Median	P value
Focal seizures Pre Post	22.55 (±79.06) 11.07 (±36.43)	0 (0-2.5) 0 (0-2)	0.38
Focal with bil tonic.clonic Pre Post	0.24 (±1.21) 0.63 (±2.15)	0 (0-0) 0 (0-0)	0.25
Tonic seizures Pre Post	38.6 (±131.46) 38.94 (±115.43)	1 (0-8.5) 1 (0-12)	0.97
Myoclonic seizures Pre Post	13.24 (±70.32) 22.93 (±96.95)	0 (0-1) 0 (0-0.75)	0.67
Spasms Pre Post	52.22 (±146.57) 44.09 (±113.16)	0 (0-9.25) 0 (0-20.5)	0.64
Absence seizures Pre Post	8.59 (±56.74) 9.33 (±55.56)	0 (0-0) 0 (0-0)	1
Focal > 5min non conv Pre Post	0.13 (±0.75) 0.11 (±0.48)	0 (0-0) 0 (0-0)	0.85

Total Carer reported seizures	N	Median	Mean	IQR	p value
Seizures baseline	40	49	159	180	
Seizures at 3 months	39	18	66	31	0.002
Subgroup analysis					
LGS Baseline seizures	12	48	98	81	
Seizures at 3 months	12	19	28	25	0.06
Dravet Syndrome Baseline seizures	5	72	195	126	
Seizures at 3 months	5	36	121	69	0.12
Non LGS No Dravet group Baseline	23	49	253	208	
Seizures at 3 months	22	14	24	88	0.019

Carers reported seizures improved at 3 months, this noted in the **non-LGS/DS groups**

Carer's reported seizures Where GIC Significant Improved	N	Median	Mean	p value
Seizures baseline	12	61	251	
Seizure at 3 months	12	8.5	86	0.01

Carers reporting **most GIC improvement** (N=12) had significant improvement in EEG seizures

Discussion

- **This study adds to sparse literature on prolonged EEG findings in those treated with CBD, and cases of EE/DEE in general**

- No change in vEEG seizures in this highly selected cohort with severe epilepsy and DEE
- However improvement of EEG seizures in those reporting significant improved GIC, may indicate some effect of CBD in a subset of patients
- Limitations with ASM changes including CLB
- Limitations with 3-month follow-up period
- Highlights the challenges of vEEG/clinical assessment in those with EE/DEE
- Types of seizures most frequently seen in this study may not = QOL (e.g. spasms, myoclonus)
- High-frequency EEG sz types may be less relevant to patient and carers
- May not be able to generalize study findings to less severe forms of epilepsy

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