Clinical Outcome Data of Children Treated with Cannabis Based Medicinal Products for Treatment Resistant Epilepsy – Analysis from the UK Medical Cannabis Registry

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Introduction

Cannabis-based medicinal products (CBMPs) are increasingly used in clinical practice for children with treatment-resistant epilepsy (TRE). However, there is a paucity of high-quality research to support the use of cannabidiol (CBD) outside of Lennox-Gastaut and Dravet syndromes. Similarly, there is limited evidence of the benefits and risks of delta-9-tetrahydrocannabinol (Δ9-THC) therapy in children with TRE.

Methods

A case series of all children (<18 years old) with TRE from the UK Medical Cannabis Registry was analysed. Primary outcomes were ≥50% reduction in seizure burden, changes in the Impact of Paediatric Epilepsy Score (IPES) and incidence of adverse events. Statistical significance was determined at a p-value<0.050.

Results

Thirty-five patients were included in the analysis (Figure 1).

Maximum tolerated daily dose of CBD and Δ9-THC are detailed in Table 1.

Twenty-three (65.7%) patients achieved a ≥50% reduction in seizure burden, whilst 13 (37.1%) sustained a ≥90% reduction in seizure burden across all treatment cohorts (Table 2). Four (11.4%) patients had complete remission. 94.1% (n=16) of patients treated with CBD and Δ9-THC observed a ≥50% reduction in seizure burden compared to 31.6% (n=19) and 17.6% (n=17) of patients treated with CBD isolates and broad-spectrum CBD products respectively (p<0.001).

There was no significant difference in IPES score between baseline and any follow-up period (p>0.050) (Table 3).

Twenty-six (74.3%) adverse events were reported by 16 patients (45.7%). The majority of these were mild (n=12; 34.2%) and moderate (n=10; 28.6%) (Table 4).

Figure 1. Pathways of treatment with CBMPs from initiation

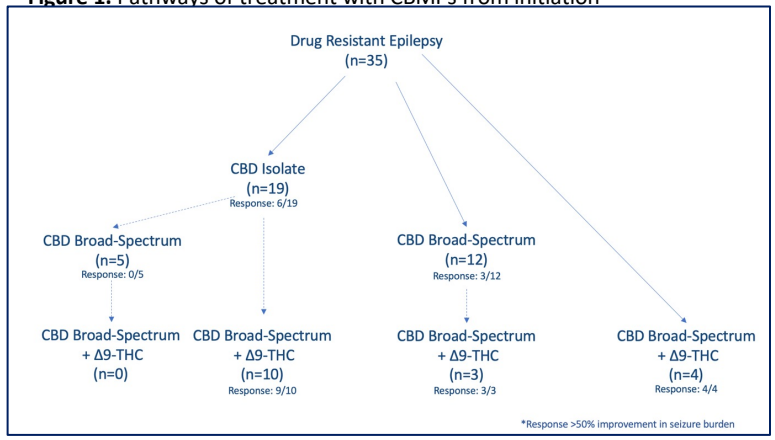

Table 1. Maximum tolerated mean daily dose for each therapy.

Cannabinoid dose (mg/kg/day)	CBD Isolate (n=19)	CBD Broad Spectrum (n=17)	CBD & Δ⁹-THC (n=17)
CBD	14.1 ± 5.3	5.7 ± 4.1	8.7 ± 4.3
Δ⁹-THC	N/A	N/A	0.4 ± 0.3

Table 2. Change in seizure frequency with maximally tolerated treatment.

Reduction in seizure burden	Maximum Titrated Therapy (n=35)	CBD Isolate (n=19)	CBD Broad Spectrum (n=17)	CBD & Δ⁹-THC (n=17)	p-value
≥50%	23 (65.7%)	6 (31.6%)	3 (17.6%)	16 (94.1%)	<0.001
≥90%	13 (37.1%)	3 (15.8%)	3 (17.6%)	9 (52.9%)	0.023
Remission	4 (11.4%)	1 (5.3%)	0 (0.0%)	3 (17.6%)	0.134

Table 3. Paired comparison of Impact of Paediatric Epilepsy Score between baseline and follow up assessment.

Follow Up Month	n	Baseline IPES Score	Follow Up IPES Score	p-value
Month 1	22	26.8 ± 5.7	24.4 ± 9.3	0.103
Month 3	12	25.2 ± 6.5	24.1 ± 9.7	0.660
Month 6	9	23.9 ± 6.5	20.2 ± 9.7	0.119

Table 4. Adverse events reported by participants (n=35)

Adverse Events	Total (%)
Anorexia	1 (2.9%)
Anxiety	1 (2.9%)
Constipation	1 (2.9%)
Fatigue	14 (40.0%)
Lethargy	1 (2.9%)
Nausea	1 (2.9%)
Seizure frequency increased	2 (5.7%)
Sepsis	1 (2.9%)
Somnolence	2 (5.7%)
Vomiting	1 (2.9%)
Weight Loss	1 (2.9%)
Total	26 (74.3%)

Conclusion

This limited case series represents the largest analysis of unlicensed CBMPs for children with TRE in Europe, providing initial insights to guide further research and carefully considered clinical practice. The reduction in seizure burden compares very favourably with the quoted incidence of ≥50% seizure reduction for anti-seizure medications in treatment-resistant epilepsy.

However, these results must be viewed in the context of a strong placebo effect previously described in randomised controlled trials for anti-seizure medications for TRE in adults and children, as well as the limitations of study design.

The short terms adverse effects appear well-tolerated, however long-term effects of CBMPs on neurodevelopment are still unknown. The UK Medical Cannabis Registry will form an important components of a pharmacovigilance strategy that will contribute to the long-term data in this patient population. The results from this study could be further utilised in the design of future phase II randomised controlled trials

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