MANAGEMENT OF PRESCRIPTION CANNABIDIOL ADVERSE EFFECTS AND DRUG-DRUG INTERACTIONS

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BACKGROUND

- Prescription cannabidiol (CBD) is approved for patients ≥1 years old with Dravet, Lennox-Gastaut, or Tuberous Sclerosis Syndromes as adjunct therapy with other anti-epileptic drugs.[1]
- More data describing longitudinal real-world use and management of prescription CBD is needed to understand post-approval outcomes.
- Specialty pharmacists evaluate the safety and appropriateness of prescription CBD therapy prior to initiation and throughout treatment and intervene to optimize therapy when needed.

OBJECTIVE

To describe the drug-drug interactions (DDIs) and adverse drug events (ADEs) experienced over the first year of prescription CBD use and their management in a real-world setting.

METHODS

DESIGN Single-center, retrospective cohort study

INCLUSION Patients prescribed CBD through the center's neurology clinic from January 2019 through April 2020

EXCLUSION Clinical trial participation or prescription CBD access or fulfillment process not completed by center's integrated specialty pharmacy

OUTCOMES
- Patient characteristics and medication use patterns
- Adverse effects and DDIs related to prescription CBD
- Management of adverse effects and DDIs

RESULTS

TABLE 1. PATIENT CHARACTERISTICS AND MEDICATION USE

	Pediatric (N=92) % (n)	Adult (N=44) % (n)
Age, years [median, (IQR)]	10 (5 – 14)	28 (21 – 44)
Gender, female	47 (43)	57 (25)
Race, white	84 (77)	86 (38)
Height, cm [median, (IQR)]	130 (102 – 147)	164 (153 – 173)
Weight, kg [median, (IQR)]	29 (17 – 38)	62 (49 –76)
Diagnosis		
Lennox-Gastaut Syndrome	89 (82)	80 (35)
Dravet Syndrome	4 (4)	5 (2)
Tuberous Sclerosis	1 (1)	2 (1)
Other	5 (5)	14 (6)
Route of administration		
By mouth	78 (72)	93 (41)
Other*	22 (20)	7 (3)

IQR = Interquartile range; *Other: G-tube, J-tube, combination of by mouth and g-tube administration

RESULTS

TABLE 2. LIVER FUNCTION TESTS

Patients in the adjacent table had both a baseline and follow-up lab without a high value at baseline. Values represent the highest value recorded within the follow-up period.

Of the patients meeting the criteria above, 25% and 20% experienced an elevated AST or ALT, respectively, at least once during the study.

	N=76 % (n)
AST Result	
High	25 (19)
In range	71 (54)
Low	4 (3)

	N=72 % (n)
ALT Result	
High	20 (14)
In range	80 (57)
Low	0 (0)

AST = aspartate aminotransferase

ALT = alanine aminotransferase

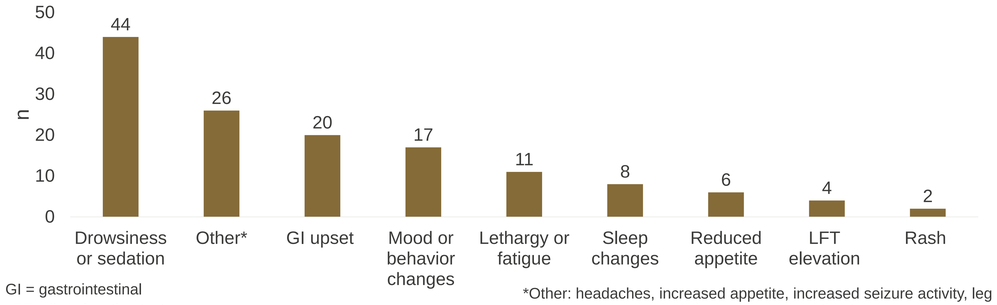
TABLE 3. DRUG INTERACTIONS (n=65)

	% (n)
Type	
Pharmacokinetic	89 (58)
Pharmacodynamic	11 (7)
Interacting Drug	
Clobazam	89 (58)
Valproic acid	5 (3)
Phenobarbital	3 (2)
Other*	3 (2)

*Other: clorazepate and a combination of clonazepam, olanzapine, and zonisamide

Pharmacokinetic interactions may cause changes in absorption, distribution, metabolism, or elimination. Pharmacodynamic interactions may cause cumulative adverse effects.

FIGURE 1. ADVERSE DRUG EVENTS REPORTED (n=138)

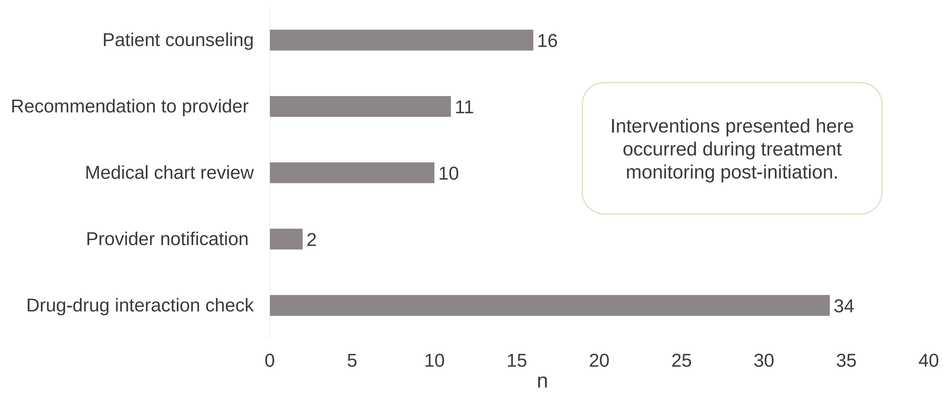


GI = gastrointestinal

LFT = liver function tests

*Other: headaches, increased appetite, increased seizure activity, leg cramps, alopecia, "digging", increased thirst, increased urination

FIGURE 2. SPECIALTY PHARMACIST INTERVENTIONS POST INITIATION (n=73)



Interventions presented here occurred during treatment monitoring post-initiation.

FIGURE 3. DRUG-DRUG INTERACTION MANAGEMENT (n=65)

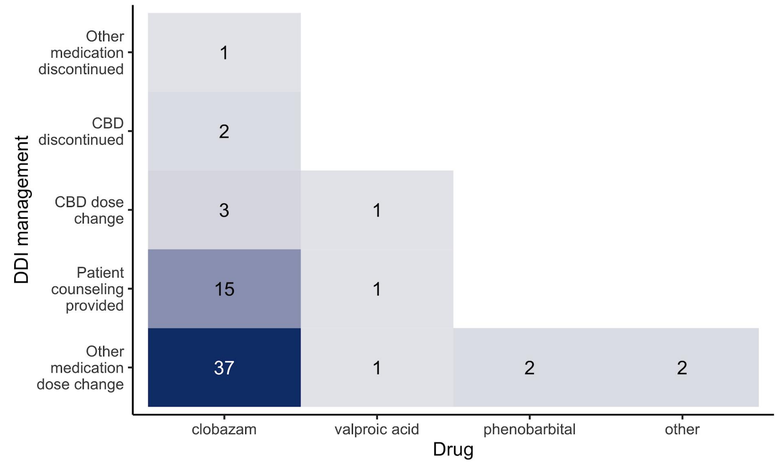
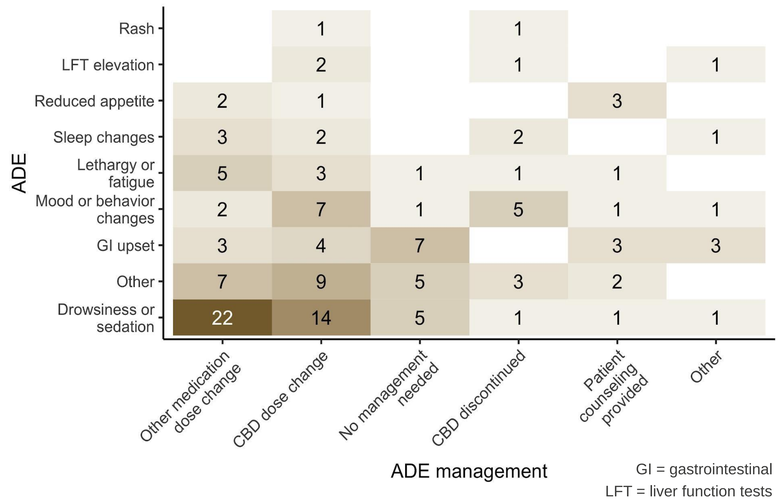


FIGURE 4. ADVERSE DRUG EVENT MANAGEMENT (n=138)



GI = gastrointestinal

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CONCLUSIONS

- In the first year of prescription CBD therapy, the most common DDI was with clobazam, which often required changing the clobazam dose.
- Drowsiness and sedation were common in the first year of therapy, which were commonly addressed by changing the dose of prescription CBD or interacting medications.
- Pharmacists play an important role in prescription CBD management by mitigating AEDs and DDIs to ensure patients can safely continue therapy.

References: 1. Epidiolex (cannabidiol) oral solution [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; April 2020. **Authors have the following to disclose concerning possible financial or personal relationships with any commercial entities that may have a direct or indirect interest in the subject matter of this presentation: Nisha B. Shah receives research grant support from Pfizer and AstraZeneca.**