MANAGEMENT OF PRESCRIPTION CANNABIDIOL ADVERSE EFFECTS AND DRUG-DRUG INTERACTIONS

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BACKGROUND

• Prescription cannabinoid (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 to intervene on 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pediatric (N=92)</th>
<th>Adult (N=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>10 (5 – 14)</td>
<td>28 (21 – 44)</td>
</tr>
<tr>
<td>Gender, female</td>
<td>47 (43)</td>
<td>57 (25)</td>
</tr>
<tr>
<td>Race, white</td>
<td>84 (77)</td>
<td>86 (38)</td>
</tr>
<tr>
<td>Height, cm (IQR)</td>
<td>130 (102 – 147)</td>
<td>164 (153 – 173)</td>
</tr>
<tr>
<td>Weight, kg (IQR)</td>
<td>29 (17 – 38)</td>
<td>62 (49 – 76)</td>
</tr>
</tbody>
</table>

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 mouth and g-tube administration

TABLE 2. LIVER FUNCTION TESTS

<table>
<thead>
<tr>
<th>Type</th>
<th>AST Result</th>
<th>ALT Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>In range</td>
<td>Low</td>
</tr>
<tr>
<td>25 (19)</td>
<td>71 (64)</td>
<td>4 (3)</td>
</tr>
</tbody>
</table>

TABLE 3. DRUG INTERACTIONS (n=65)

<table>
<thead>
<tr>
<th>Type</th>
<th>% (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacokinetic</td>
<td>89 (58)</td>
</tr>
<tr>
<td>Pharmacodynamic</td>
<td>11 (7)</td>
</tr>
<tr>
<td>Interacting Drug</td>
<td>Clobazam</td>
</tr>
<tr>
<td>89 (58)</td>
<td>5 (3)</td>
</tr>
</tbody>
</table>

*Other: clonazepam and a combination of clonazepam, diazepam, and zonisamide

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

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

- Drowsiness or sedation: 44
- GI upset: 26
- Mood or behavior changes: 20
- Lethargy or fatigue: 17
- Sleep changes: 11
- Reduced appetite: 8
- GI upset: 6
- LFT elevation: 4
- Rash: 2

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

- Recommendation to provider: 16
- Medical chart review: 11
- Drug-drug interaction check: 34

Interventions presented here occurred during treatment monitoring post-initiation.

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

- Other medication discontinued: 1
- CBD discontinued: 2
- Patient counseling provided: 15
- Other medication dose change: 37

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

- Rash: 1
- Reduced appetite: 1
- Sleep changes: 1
- Lethargy or fatigue: 1
- Mood or behavior changes: 1
- GI upset: 1
- Other: 1
- Drowsiness or sedation: 1

- GI = gastrointestinal; LFT = liver function tests

CONCLUSIONS

• In the first year of prescription CBD therapy, the most common DDI was with clobazam, which often changed the dosing of the interacting medications.
• 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 ADEs and DDIs to ensure patients can safely continue therapy.

References: 1. Epidiolex® [package insert] [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; April 2020. Authors have the following disclosures 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: Wisha B. Shah receives research grant support from Pfizer and AstraZeneca.