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EFFICACY AND SAFETY OF EPIDIOLEX (CANNABIDIOL) IN CHILDREN AND YOUNG ADULTS WITH TREATMENT-RESISTANT EPILEPSY: UPDATE FROM THE EXPANDED ACCESS PROGRAM

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Content:

RATIONALE:
Cannabidiol (CBD) is the most abundant non-psychoactive cannabinoid in the cannabis plant. Animal studies demonstrate anticonvulsant efficacy in multiple species and models. Anecdotal reports suggest efficacy in children with treatment-resistant epilepsies (TRE), including Dravet Syndrome (DS) and Lennox-Gastaut Syndrome (LGS). We report current results in our expanded access treatment program.

METHODS:
Children and young adults with TRE in an expanded access compassionate use program for CBD were enrolled in a prospective observational study. During the 4 week baseline, parents/caregivers kept prospective seizure diaries of all countable motor seizure types. Patients received a highly standardized pharmaceutical plant-derived, purified CBD. (Epidiolex: GW Pharma), at a gradually increasing dose from 2-5 mg/kg/day until intolerance occurred or a maximum dose of 25 mg/kg/day was achieved. Patients were seen at regular intervals of 2-4 weeks during the initial 12 weeks of therapy. Testing for hematologic, liver, kidney function and AED levels was performed at baseline, and after 4, 8 and 12 weeks of CBD therapy.

RESULTS:
261 patients received at least 3 months of treatment and had available data at last group data collection (136 (52%) were male; average age 11.8 years, range 4 months-41 years; average weight 38 kg; range 6.4-127). The most common diagnoses were DS (44; 17%) and LGS (40; 15%). The average # of concomitant AEDs was 3.0. After 3 months of therapy, the median overall seizure frequency reduction was 45.1% in all patients and 62.7% in DS patients. For LGS patients, the median reduction of atonic seizures from baseline was 71.1%. Among all patients, 47% had a ≥50% reduction in seizures. Seizure-freedom at 3 months occurred in 9% of patients and 13% of DS patients. Clobazam co-therapy was associated with a higher rate of treatment response (≥50% convulsive seizure reduction): 57% v. 39%; this may reflect elevations in the desmethyl clobazam metabolite. Safety data from 313 patients representing 180 patient years was available at 16 sites. Adverse events in ≥10% of patients included somnolence (23%), diarrhea (23%), fatigue (17%), decreased appetite (17%), convulsions (17%) and vomiting (10%). 14 patients (4%) had an adverse event leading to discontinuation of CBD. 36 patients (12%) withdrew primarily due to lack of efficacy. Serious Adverse Events (SAEs) were reported in 106 patients (34%), including 7 deaths, none of which were considered treatment-related. 16 patients (5%) had SAEs that were considered treatment-related, including altered liver enzymes (4 pts; all were also on valproate and clobazam), status epilepticus/convulsion (4), diarrhea (4), decreased weight (3), thrombocytopenia (1), and others.

CONCLUSIONS:
These results from an uncontrolled study support the animal studies and prior reports showing that CBD may be a promising treatment for TRE and it is generally well-tolerated in doses up to 25mg/kg/day. Epidiolex is now being investigated in randomized controlled studies in DS and LGS.