Iowa Specialty
Hospitals & Clinics

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January 19, 2019

Iowa Board of Medicine
400 SW Eighth Street, Suite C,
Des Moines, Iowa 50309

Dear Board of Medicine,

I am writing in support of 4241 C Standards of practice - medical cannabidiol, to now include severe autism as an approved condition for the receipt of cannabidiol through the Iowa Medical Cannabidiol program

I have been to many national autism meetings for physicians, where treating doctors from other states have reported in case studies where medical cannabidiol has been reported effective for the patients.

There are only two FDA approved medications for autism, Risperdal and Abilify. Physicians, like myself, who treat children with autism are often queried by the parents if 'medical marijuana' would be helpful for their child. It would be an advantage to be able to offer this treatment option for those patients with severe autism.

I strongly encourage the Board of Medicine to approve severe autism as certifiable condition for medical cannabidiol.

Sincerely,

Jon Ahrendsen MD

Jon Ahrendsen MD

MENTAL HEALTH

Marijuana among agents used to calm kids with autism

BY M. ALEXANDER OTTO
EXPERT ANALYSIS AT THE PSYCHOPHARMACOLOGY UPDATE INSTITUTE

SAN FRANCISCO – About once a month, Antonio Y. Hardan, MD, and his colleagues at the Stanford (Calif.) University Autism and Developmental Disorders Clinic see an autistic child who is using or being prescribed marijuana.

"There are two types or responses we see with marijuana," said Dr. Hardan, director of the clinic. "Most of the time, it calms the kid down for 2 or 3 hours, which is what you'd expect from marijuana. In 1 out of 10, I am hearing that parents see improvements in the core features of autism. We have several families who would swear by marijuana, but then 4 or 6 months later, they will change their mind and say it's not helping as much.

"We are very interested in doing a trial with marijuana," Dr. Hardan said, but the jury is still out. "There are three companies that are making regulated dosages that would allow us to study it in a very reasonable way. Hopefully, in the future, we will be able to provide some information about this," he said at a psychopharmacology update held by the American Academy of Child and Adolescent Psychiatry.

Marijuana is just one of many alternatives families and doctors are trying to improve upon the usual medications and therapies for autism; the range of options being tried speaks to the desperation and frustration of families looking for help. There's no home run so far; the common denominator for alternatives is anecdotal support but little evidence. Stanford has tried to address the evidence gap and continues to do so, Dr. Hardan said.

In 2012, for instance, he and his colleagues reported a 33-patient study that found that *N*-acetylcysteine (NAC) – another hopeful candidate in recent years – might curb irritability (Biol Psychiatry. 2012 Jun 1;71[11]:956-61).

Dr. Antonio Y. Hardan

The tricky part about NAC is that it's a dietary supplement, so you can't be sure of what you're getting in the store. There were questions at the talk about dose and formulations.

"The one we used in the study is made by BioAdvantex," a Canadian company. "That's the one that worked for us. One of the advantages is that every dose is wrapped individually." NAC is an antioxidant, "so if you expose [it] to oxygen or light, it will get oxidized, and over time be less effective," said Dr. Hardan, also professor of psychiatry and behavioral sciences at the university.

Most of the time, NAC is very well tolerated, with only a little bit of flatulence and upset stomach.

Dr. Hardan and his colleagues started with 900 mg in one dose once a day for 4 weeks, then one dose twice a day for 4 weeks, followed by one dose three times daily, in children aged 2-12 years old. With experience, they are going faster now, cutting the 4-week interval to 2. "Some people are [even] more aggressive, which is okay," he said.

Propranolol is another fashionable option, prescribed by a lot of doctors.

It's not a new option; about 20 years ago, "we used it in very high dosages, 700-800 mg a day for self-injurious behavior. People wonder how you can go that high; above a dose of 200 mg, there is what we call an 'escape phenomena' where the heart will stop responding, and the effects on blood pressure and pulse are minimal," Dr. Hardan said.

Interest in propranolol over the past 5 years has expanded to anxiety, sensory abnormalities, and other nonspecific autism symptoms. "Unfortunately, there are no clinical trials to support that," he said. The only evidence so far is from a functional MRI study in adults that suggested a little bit more efficient processing on a language task; further investigation is underway.

Many parents also are asking for oxytocin, and doctors are prescribing it. Someone in the audience wondered whether it had a role in everyday practice. "Not at this time," Dr. Hardan said. "I would suggest waiting a little bit until" results are reported from an ongoing trial. They are due soon, and there might be a subgroup of kids who benefit. Oxytocin seemed to help all-comers recognize facial cues.

Arginine vasopressin might do that, too, and be more specific for autism; Stanford is planning a study to look into it. Attendees also wanted to know what to do about sleep problems, a common issue in autism.

"I'm aggressive in the treatment of insomnia, especially in single-parent households, because if the kid isn't sleeping, the parent isn't sleeping" and they may get irritable and moody, which raises the risk of abuse, Dr. Hardan said.

He said he starts with melatonin, 1 mg in the evening, and increases it by 1 mg every week to hit a target of 6 mg per night. He said he hasn't seen much benefit of going higher. It's important to remember that melatonin might take up to a week to see the full effect. If melatonin fails, Dr. Hardan goes up the ladder. Diphenhydramine (Benadryl), benzodiazepines, trazodone (Oleptro), and mirtazapine (Remeron) are among the options. Rarely, there's a need for quetiapine (Seroquel). To counter benzodiazepine disinhibition, he said he asks parents to try them on a good day at home, so the effects of environmental stressors like going to the dentist can be separated from those of the drug.

> "We have several families who would swear by marijuana, but then 4 or 6 months later, **they will change their mind** and say it's not helping as much."

Dr. Hardan cautioned that there is "no evidence at this time to support the use of" lamotrigine (Lamictal). "Please don't use it; somebody will end up developing" Stevens-Johnson syndrome. "It will be difficult to defend against that."

Dr. Hardan is an adviser for Roche.

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January 20, 2019

Iowa Board of Medicine
400 SW Eighth Street, Suite C
Des Moines, Iowa 50509

Dear Board of Medicine,

I am writing in support of 4241 C Standards of Practice- medical cannabidiol, to now include severe autism as an approved condition for the receipt of cannabidiol through the Iowa Medical Cannabidiol program.

At the Medical Doctor's Conference on Cannabis as Medicine, November 2016 in Denver, CO, Dr Christian Bogner presented articles supporting the use of cannabis in Autism. These can be found on the website www.mammausa.org, under The Science Link with references. Below is an excerpt:

" The endocannabinoid system appears to be directly impacted by, as well as a potential target for treatment of, physiological manifestations of genetic factors associated with ASD including NL3 mutations and FXS (Fragile X). NL3 mutations inhibit tonic secretion of endocannabinoids and disrupt their signaling. This possibly contributes to the identified increase in pro-inflammatory cytokines levels in ASD. CB2 is upregulated in the brain in response to inflammatory stimuli as part of a neuroprotective role , and is suggested as a target for treatment. There appears to be a preponderance of evidence that the ECS is involved in the progression of ASD. "

I have attended yearly national medical conferences on Autism since 2005. Improving short and long term functioning of individuals with autism spectrum disorder is a common goal of both parents/caregivers and health care professionals. As a Physician Assistant practicing in Iowa, many parents whose children have failed multiple pharmaceutical and behavioral interventions, have inquired if medical marijuana would be an option to trial for their child's aggression and severe autistic symptoms. I believe parents and physicians in Iowa should have the right and legal protection to explore medical cannabis as a treatment option, especially in severe autism.

Sincerely,

Karn J Johansen PA-C
Iowa Specialty Hospital- Clarion Clinic