INTRODUCTION

- Autism Spectrum Disorder (ASD), Fragile X Syndrome (FXS), and 22q11.2 deletion syndrome (22qDS) are complex neurodevelopmental conditions with considerable overlap in neurophysiological and behavioral symptomatology.

- ASD is characterized by problems in social communication and social interaction, as well as restricted and repetitive patterns of behavior, interests, or activities.

- FXS is a rare genetic condition caused by CGG repeat expansion in the FMR1 (fragile X mental retardation 1) gene located on the X chromosome; behavioral symptoms may include social withdrawal, anxiety, avoidance of eye contact, sensory hypersensitivity, echolalia, and hand flapping.

- 22qDS is one of the most common microdeletion syndromes, and it often involves behavioral symptoms of social limitations and difficulties in maintaining relationships with peers.

- The socio-behavioral deficits seen in ASD and FXS have been attributed to dysregulation of the endocannabinoid system, which is composed of:
  - Two G-protein-coupled receptors
  - Cannabinoid receptor type 1 (CB1) – located primarily in the CNS
  - Cannabinoid receptor type 2 (CB2) – located in multiple systems throughout the body

- Endogenous cannabis-like ligands (endocannabinoids) that bind to CB1 receptors and modulate synaptic transmission throughout the CNS; the two best described are:
  - Anandamide (AEA)
  - 2-arachidonoylglycerol (2-AG)

- Cannabinoid (CB) is a non-euphoric cannabinoid

- Autism Spectrum Disorder (ASD), Fragile X Syndrome (FXS), and 22q11.2 deletion syndrome (22qDS) are their respective diagnostic criteria.

OBJECTIVE

- The objective of this study was to conduct a retrospective literature review on patients with ASD, FXS, and 22qDS to determine the nature and extent of symptomatic overlap in these conditions and to suggest a possible role for CBD in the management of these shared symptoms based on insights from our open-label, 12-week study evaluating the safety, tolerability, and efficacy of transdermal CBD for the treatment of behavioral and emotional symptoms associated with child/adolescent FXS.

METHODS

- A search of the PubMed database was conducted using the terms “behavior,” “behavioral symptoms,” “autism spectrum disorder,” “ASD,” “Fragile X Syndrome,” “FXS,” “22q11.2 deletion syndrome,” “patients,” “caregivers,” and “CBD” and treatment of anxiety” with no restriction on date or publication type.

- Records were analyzed for relevance.

RESULTS

ALL CONDITIONS

- The most common behavioral manifestations across all conditions are anxiety-related; such as social avoidance, irritability, attention deficits, stereotypy, poor communication, and social unresponsiveness (Figure 2).

- Anxiety-related symptoms are common in patients with ASD, with up to 84% of children experiencing some degree of debilitating anxiety; rates of physician-diagnosed anxiety disorders range from 42-55%14,15 and may include simple phobias, generalized anxiety disorder, separation anxiety disorder, obsessive-compulsive disorder, and social phobia.

- Comorbid anxiety disorders can be broad-ranging and associated with behaviors such as aggression/irritability and isolation from same-age peers16.

- Inattention and hyperactivity are often present in Attention-Deficit/Hyperactivity Disorder and ASD, and they are common to their respective diagnostic criteria.

- Children with ASD who have severe intellectual disability (ID) (IQ<40) showed higher levels of psychiatric symptoms (anxiety, mood, sleep, organic syndromes, and stereotypies/tics) than those with ID but no ASD17.

- FXS is in FXS, severe cognitive and social impairments are more common in males than in females18.

- FXS usually has profound effects on the life of patients (comorbid conditions, social impairment) as well as their caregivers and families (mental health, absence from work/school), and it is generally well tolerated in children and adults33,34.

- Literature review, CBD may improve multiple symptoms experienced by patients with ASD, FXS, and 22qDS, and it is well tolerated in children and adults1.

- Preliminary evidence shows that CBD improves social anxiety and associated behavioral withdrawal, anxiety, avoidance of eye contact, sensory hypersensitivity, echolalia, and hand flapping3.

- In ASD, severe cognitive and social impairments are more common in males than in females.

- In FXS, symptomatology manifests more as self-harming behaviors (eg, self-injurious behavior, self-mutilation).

- In 22qDS, and it is generally well tolerated in children and adults.

- Although these diagnoses are reported in individuals with 22qDS, the diagnosis of ASD is particularly controversial in this population and may be related to poor clinical understanding of the typical behavioral phenotype.

- The emergence of social deficits during adolescence can represent a major source of disability in some individuals with 22qDS; cross-sectional studies show that children with 22qDS2,29,30.

- Are withdrawn and shy

- Have social impairments which may be less of a concern to the individual

ROLE OF CBD

- CBD has diverse pharmacologic effects.

- Based on our findings from the open-label study in children/adolescents with FXS4 and FXS and 22qDS, we believe that further research is needed to establish the role of CBD as a treatment for anxiety and related behavioral symptoms in this population.

- The most common behavioral/psychiatric diagnoses in children with 22qDS are ADHD, ASD, and anxiety.

- A recent case series provided initial evidence that CBD may lead to broad improvement in childhood symptoms of anxiety, aggression/irritability and isolation from same-age peers.

- In FXS, severe cognitive and social impairments are more common in males than in females.

- In 22qDS, symptomatology manifests more as self-harming behaviors (eg, self-injurious behavior, self-mutilation).

- Although these diagnoses are reported in individuals with 22qDS, the diagnosis of ASD is particularly controversial in this population and may be related to poor clinical understanding of the typical behavioral phenotype.

- The emergence of social deficits during adolescence can represent a major source of disability in some individuals with 22qDS; cross-sectional studies show that children with 22qDS2,29,30.

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Conclusions

- Patients with ASD, FXS, and 22qDS share a constellation of socio-behavioral symptoms that includes anxiety, leading to seeking isolation behavior (social avoidance), irritability, attention deficits, and poor communication.

- Preliminary evidence shows that CBD improves social anxiety and associated behavioral manifestations suggesting that it may prove to be effective in managing the spectrum of behavioral symptoms associated with these conditions.

References


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