angelman SYNDROME FOUNDATION

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WITH YOU FOR THE JOURNEY.

To Whom it May Concern:

This individual has been diagnosed with a rare neurogenetic disorder called Angelman syndrome (AS). AS is caused by a loss of the maternally expressed UBE3A gene. This is most commonly due to a deletion of the Angelman critical region on the maternal copy of chromosome 15q11.2-13.1, but there are other genetic mechanisms as well. ***Individuals with Angelman syndrome are at high risk of developing seizures, particularly in the setting of febrile illnesses in childhood.*** As many as 85-90% of children with AS will develop seizures by 3 years old. Children with Angelman syndrome often present with atonic or drop seizures but can have generalized tonic-clonic, focal or other seizure types as well. This letter is meant to provide general guidelines for treatment of seizures in Angelman syndrome, however each child is unique and may not respond to the typical medications used in AS.

Prolonged seizures or not returning to baseline between brief seizures:
Benzodiazepines work very well for stopping seizures in individuals with Angelman syndrome and should be considered first line. Depending on clinical status, oral versus IV or intranasal preparations can be utilized and in the typically recommended weight based dosing for children and standard dosing for adults.

Usually effective & well tolerated initial daily medications for outpatient management of new onset seizures:
Levetiracetam (Keppra)
Clobazam (Onfi)

Less desired medications: Valproate (aka Depakote, Depakene, valproic acid)
In a large series, “patients on valproic acid therapy exhibited increased tremor, decreased balance and/or regression of motor skills, which resolved after tapering off of this medication” (Thibert, Epilepsy Behavior 2016)

All patients with Angelman syndrome who have had a first time seizure should be provided with a prescription for seizure rescue medications which can include rectal diazepam (Diastat), intranasal diazepam (Valtoco approved for 6yo and older in 2020), intranasal midazolam (any form and Nayzilam is approved for 12yo and older) and in some countries buccal midazolam products are available for rescue therapy.

It is important to recognize that this is a rare genetic syndrome and often times parents are the first to recognize clinical decline in their children and should be taken seriously when concerned for seizures as they are so pervasive in this condition. Delay in treatment can lead to development of nonconvulsive status epilepticus (NCSE), which can often be managed as an outpatient as well. Please see attached guidelines for outpatient management of NCSE as adapted from the extensive experience of the Angelman team at Massachusetts General Hospital. For urgent consultation with a neurologist who specializes in the management of seizures in Angelman syndrome, please email clinics@angelman.org. This email is monitored daily between 8AM - 8PM and we are happy to facilitate expert consultation in a timely manner. (Coming soon a 24 hour seizure hotline that can be used to consult with AS expert).*

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