CdLS Foundation
Cornelia de Lange Syndrome Foundation, Inc.

Pharmacotherapy in CdLS

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Psychotropic medication use in individuals with CdLS should be dictated by specific symptom targets. As in other individuals with developmental disabilities, target symptoms tend to fall into four specific symptom categories:

Category I: Hyperactivity/Hyperarousal (Attention Deficit Hyperactivity Disorder (ADHD))

Category II: Anxiety/Negative Affect (anxiety/depression)

Category III: Major Mood Instability (bipolar disorder)

Category IV: Disorganized Behaviors/Aggression/Self-Injury (psychosis)

For example, a child with CdLS may present with disruptive behaviors, mood swings and self-injury. When the child is examined, it is usually the case that a single symptom category is the most prominent. The identified symptom category can then guide pharmacologic (medication) treatment. Likewise, it is not expected that a psychotropic (psychiatric medication) can improve more than one symptom category.

The behavioral symptom categories, in turn, correspond to specific psychotropic groups, so that once the target symptom is identified, the medication choice can follow.

- Hyperactivity and hyperarousal can be treated with psychostimulants such as methylphenidate (Ritalin, Concerta, Metadate, Ritalin LA and others) and dextro-amphetamines (Dexedrine, Adderall, Vyvanse, and others). Common side effects are loss of appetite and insomnia; disorganization in children with disabilities can also occur.
- Also effective is the non-stimulant atomoxetine (Strattera), as well as alpha-agonists such as clonidine (Catapres) or guanfacine (Tenex, Intuniv [a long-acting form]). Common side effects of alpha-agonists are sedation and hypotension (low blood pressure).
- Anxiety and depression can be treated with a selective serotonin reuptake inhibitor (SSRI) such as fluoxetine (Prozac), sertraline (Zoloft), fluvoxamine (Luvox), citalopram (Celexa), escitalopram (Lexapro), or paroxetine (Paxil). All SSRIs have convincing efficacy data for depression and anxiety in adults, but only fluoxetine has shown convincing efficacy in depressive disorders in children, so it may have a slight advantage

over others. Side effects with SSRIs are restlessness with agitation, insomnia and behavioral disinhibition (impulsiveness, poor judgment). Other minor side effects are headaches and insomnia.

- Benzodiazepines (diazepam [Valium], lorazepam [Ativan], clonazepam [Klonopin] and others) are not routinely used in children due to a tendency to either behaviorally disinhibit or sedate excessively. Due to its long half-life, Clonazepam may have more effectiveness in treating anxiety long-term.

Other antidepressants can be used, such as trazodone (Desyrel, aids in sleep), venlafaxine (Effexor, aids in increased energy) or mirtazapine (Remeron, aids in sleep and appetite). Tricyclics, such as imipramine and nortriptyline, are more problematic because heart rhythms and blood levels need monitoring; however, they are as effective as other antidepressants.

- Overall, there is sparse data to guide use of antidepressants in individuals with developmental disabilities; however, with cautious use they can be effective in treating anxiety and depressive disorders. Major mood problems can be treated with mood-stabilizers such as lithium (Lithium Carbonate, Lithobid and others), carbamazepine (Tegretol), oxcarbazepine (Trileptal) or valproic acid (Depakote). Except for lithium, all others are anti-convulsants to some degree, addressing a biological connection between major mood symptoms and ion channel instability (a cause of seizures).

Second-line options are lamotrigine (Lamictal) and gabapentin (Neurontin). Organ damage (kidney, liver) is rare, but possible with these medications. Blood tests monitor the drug levels.

- Disorganized behavior, aggression and self-injury can be treated with neuroleptics such as risperidone (Risperdal), olanzapine (Zyprexa) and quetiapine (Seroquel), among others. While these are popular options for disruptive behaviors, potential side effects are also highly probable, and range from akathisia (constant movement) to metabolic syndrome (hyperinsulinemia, diabetes) and weight gain.

In general, the side effect profile is more problematic when moving from a Category I to a Category IV medication, therefore consideration should be given to lower categories when using psychotropics. Finally, the following guidelines should be kept in mind when considering such medication for behavior management in individuals with CdLS:

- There is no drug safety data specific to CdLS, so predictions from non-developmentally delayed adults, and sometimes children, have to be made when considering a drug's safety profile.
- There appears to be a host of unusual and unexpected side effects observed in individuals with CdLS who use psychotropics (for example, agitation with risperidone). This may be related to the little understood and unique underlying biology in CdLS. A good rule is to start low and go slow when using psychotropics in individuals with CdLS.

All inquiries about medications can be directed to the CdLS Foundation via the Ask the Expert feature of the Web site (www.CdLSusa.org) or by calling a family service coordinator at 800-753-2357.

If you would like to participate in a Foundation-approved survey regarding psychotropic medications used in CdLS, contact Dr. Grados at 443-287-2291 or mjgrados@jhmi.edu. *The research aims to help better understand the effects of these medications to manage behaviors that can greatly affect the quality of life for children and families.*