Behavioral Medications and MPS Diseases

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Presently there is little empirical evidence to support the use or efficacy of using medications to address behavioral issues in children with MPS diseases. This, however, has not limited the use of behavioral medications and the success in certain individuals. The most common behaviors treated with medications in non MPS populations are attention, concentration, impulsivity, hyperactivity and sleep disturbance. In addition, mood symptoms such as depression, anxiety, mood swings, raging (intense anger outbursts), agitation and irritability may also be successfully mediated with medication.

Every physician or psychiatrist should consider the following questions before treating any patient with psychotropic medications:

- Given the complexity of MPS and related diseases, should the doctor treat the patient with MPS?
- Will psychotropic medication help?
- Are there any risks to the use of psychotropic medication in this patient?
- Do the benefits outweigh the risks?
- What is the desired outcome?
- What is a reasonable timeline to determine efficacy of a medication trial?

These questions can be rather difficult to answer given the prevalence of MPS diseases in the general medical and psychiatric community. It has been reported that when positive behavioral and mood changes are observed, dosages used in children with MPS are much higher in some circumstance that in non MPS individuals (Wraith, E). Given the lack of information currently available to physician or psychiatrist willing to treat an individual with MPS with psychotropic medication, the approach is often one based on trial and error.

Every parent should consider the following questions before treating their child with psychotropic medications:

- What is the specific desired outcome?
- Do we mutually agree on the desired outcome?
- What are reasonable behavioral expectations for my child?
- What are the effects of this medication?
- What are the side effects of this medication?
- What are the specifics of this medication trial (days, weeks, etc)?
- Am I willing to be consistent with this pharmacological trial?
- Do I have regular access to my doctor so I can discuss observations during this trial?

What are the potential behaviors that psychotropic medication addresses in a typically developing child?

- Hyperactive, "motor driven" behavior, where you see children on the go with a very short attention span, flitting from object to object, subject to subject, often with no apparent purpose and non-stop.
- Physical aggressions occasionally with property destruction
- Noncompliance with instructions absent a sense of danger.

This is a fairly typical pattern of behavior in MPS II & III and is a challenging issue for caregivers and parents to address and modify.

Medication is only one component in the development of effective strategies to manage challenging behavior.

A comprehensive behavioral assessment can be helpful to parents and caregivers. Identification of variables both inside and outside the home that may reinforce challenging behavior can aide in the development of tailored strategies. Despite the lack of empirical evidence to support of their use in changing target behaviors, the information can be used as a baseline to help determine the effectiveness of medication trials.

Environmental modifications are important in the development of strategies to address and modify challenging behaviors (put your television out of reach, or your video on the top shelf and don't have your breakable ornaments within reach etc). Such changes not only help to create a safer environment for your family but can serve to reduce stress on parents and caregivers who are always required to be on guard for safety reasons.

There are several different drugs that can be tried to assist in the development of a plan to address challenging behavior.

Medication Class	**Targeted Behaviors or Symptoms**
Antipsychotics	delusions, hallucinations, aggressive dangerous behaviors, mood swings, mania
Anxiolytics	anxiety, insomnia
Antidepressants	explosive episodes, mood diseases, emotional instability, depression, anxiety, impulsivity
Anticonvulsants	mood swings, irritability, headache, frustration tolerance
Stimulants	attention, impulsivity, hyperactivity, focusing
Mood Stabilizers	explosive episodes, emotional instability

When you see lists like this, with different types of medications addressing similar behaviors or symptoms, it becomes apparent that the intended effect of the medication you decide to use is not a guarantee. Parents often find it difficult to accept that, in some circumstances, doctors are not able to successfully treat the child's challenging behavior with the use of medication.

Antipsychotics

This class of medication can cause drowsiness initially but generally subsides with continued treatment or decreasing the dosage. More serious concerns regarding the use of antipsychotic medications are a variety of movement diseases such as dystonia, akathisia, parkinsonism and tardive dyskinesia. Each of these can be a direct side effect of using a typical antipsychotic medication and often remits when medication is discontinued. When used successfully, this class of drug can result in a reduction of active behavior.

There are newer antipsychotic medications (second and third generation antipsychotic medications) developed in recent years that do not have the same risks as earlier versions. These newer medications may help avoid the risks associated with older versions, however, selection should be guided by a clear plan of targeted symptoms and a thorough understanding of associated monitoring. Certain medications require regular blood work to monitor appropriate levels for liver and thyroid functioning.

Anxiolytics

There are two classes of the anxiolytics, benzodiazepines and serotonin agonists. The benzodiazepines are used commonly in patients with MPS specifically when associated with an event (like a medical procedure) that is short term and causes situation specific anxiety. This class of medication can suppress aggression, sedate patients and reduce anxiety. They also have anticonvulsant and muscle relaxing properties. Children who have an excessive amount of motor activity, muscle spasms or twitching may experience relief from these behaviors.

An important consideration with regard to the side effect of the benzodiazepines is the increased levels of secretion which occur in many patients. This can pose a significant difficulty in an MPS individual with poor swallowing. As a result, this side effect may actually limit the use of this type of medication in certain patients.

Drowsiness and confusion are the most common side-effects seen in clinical practice. This is also a class of medication that you need to be mindful of *tolerance*. Dosages need to be increased over time to achieve the same effect. Addiction and tolerance are not the same. Over time patients will metabolize the medication faster and need a larger amount to get the same effect. It is also important to remember if you have taken benzodiazepines for a long time, you need to withdraw them carefully and slowly. *Seizures* are a significant risk factor if you discontinue abruptly. Respiratory depression is another problem to watch out for.

The serotonin agonists may be used to treat anxiety that is ongoing, long term or more generalized in nature. This class has fewer sedating effects and causes less cognitive impairment. The main disadvantage of this class of medication is that it takes several weeks before its anxiolytic effect become noticeable.

Antidepressants

This class of medication is aimed at addressing mood symptoms such as depression, lethargy, apathy, anxiety and impulsivity. They can be useful in some children who have mood disturbance. Great caution must be taken in patients with seizure diseases that are not effectively managed. There are two common groups of antidepressants which have been widely for children with MPS diseases. They are the tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs).

There is anecdotal evidence to support the use of the tricyclic antidepressant Imipramine. It has been the treatment of choice for a particular form of epilepsy known as gelastic epilepsy (a subtype of epilepsy induced by laughing).

There are some anecdotal reports of success with the SSRIs such as Prozac. Some children with MPS II and MPS III can have wildly fluctuating mood marked by crying or laughing without external causation. An SSRI may stabilize and lighten mood in some patients with MPS. It can be difficult to discern unprovoked emotions (crying or laughing) from actual pain. As such, confirmation with your treatment team is essential.

An important consideration with using antidepressants is use with a child with uncontrolled seizures. In some patients antidepressants can exacerbate seizures.

Anticonvulsants

These medications can be used for treating challenging and impulsive behavior. They are commonly used in seizure diseases, for neurologically based pain, for anxiety and have been found to have mood stabilizing properties. They are a diverse group of medications that span a variety of different classes of drugs (i.e., barbiturates, benzodiazepines). As such the side effects will vary significantly depending on which medication is selected for use but may be a good choice for children with seizure activity that is uncontrolled.

Psychostimulants

This class of medication is commonly used in the non MPS population in the management of hyperactivity, challenging behavior and/or Attention Deficit Disease. These are typically used adjunctively with therapy, specifically behavior modification and parent training, in children who have motor-driven behavior, inattention and impulsivity.

Stimulant medication is short acting. The effects can be seen within the hour and can last from 4 to 8 hours. An important consideration in using stimulant medication is loss of appetite which can lead to weight loss. Careful consideration is needed if a pre existing cardiac condition exists. These medications are schedule II controlled substance and carry with them a high risk for abuse and addiction.

Recently a non stimulant (Atomoxetine) medication has been approved and used successfully in non MPS children. This medication is longer acting (24 hours) has less addictive potential and risk for abuse.

Mood Stabilizers

There is no research or anecdotal evidence at this time to support the use of mood stabilizers in MPS children to address difficult or challenging behavior that is not directly the result of a confirmed diagnosis of Bipolar disease.

These medications are used to treat rapidly shifting and intense mood shifts and bipolar disease (mania and depression). Lithium is one of the most widely known mood stabilizers. Other medications used and considered to have mood stabilizing properties come from the group of anticonvulsant and the antipsychotic medications.

Common side effects can include lethargy and weight gain. Some medications in this group may require additional testing to monitor adequate liver functioning.

Summary

It is important after your child's medical and behavioral evaluation to talk with the physician about behavioral medications and what is recommended for your child. Not all children with an MPS disease have the same benefit or reaction from a specific medication. If a medication is not beneficial, it should be stopped and another considered. The National MPS Society does not endorse specific medications.