

Summary – Psychiatric Disorders & Mitochondrial Disease

Dr. Marcus Favero

Introduction

Dr. Marcus Favero is a clinical instructor of psychiatry at Harvard Medical School and a psychiatric clinician at Massachusetts General Hospital in Boston. He is board certified in Pediatric, Adolescent and Adult Psychiatry and has a special interest in patients with Mitochondrial Disease. His discussion will focus on the connection between psychiatric disorders and Mitochondrial Disease.

History

Mitochondrial Disease is a very new disease. Studies began in the 1960's; association with abnormal neurological function began in the 19670's and continued through the 1990's. It was not until 2000 that there was real recognition of the clinical conditions of Mitochondrial Disease - that is only 10 years ago. It is now known that Mitochondrial Disease is the most prevalent of the metabolic disorders. We still know very little about Mitochondrial disorders but referrals to MGH are increasing our knowledge of the connection between psychiatric and mito diseases. Of all the metabolic disorders, mito is the most under appreciated and under diagnosed. It is important to note that trying to treat both a mitochondrial disorder and a psychiatric disorder can be very complicated. Yet, psychiatrists know very little about Mitochondrial Disease. Dr. Favero emphasizes that it is important for psychiatrists to be educated about mitochondrial disease and other metabolic disorders. Otherwise, psychiatric disorders may be wrongly managed.

General Management

The prevalence of psychiatric disorders in patients with Mitochondrial Disease is fairly high and the treatment of psychiatric diseases can decrease the metabolic stress, therefore alleviating some symptoms of Mitochondrial Disease. If a patient and his/her family is less stressed, then they are more likely to adhere to the nutritional supports needed for successful Mito care. Psychiatric distress causes metabolic stress, so it is important that Mito patients seek help for psychiatric disorders. Before any medication is prescribed, Dr. Favero advises that patients seek out other alternatives first. Psychiatrists can also provide therapeutic help so that the medical doctor does not have to take on the additional role of counselor. However, care must be taken in the use of psychiatric medications when working with Mitochondrial Disease.

What Can a Psychiatrist Do?

First of all, a psychiatrist needs to make an accurate diagnosis. The psychiatrist must assess the extent to which the symptoms are primary (they would be present without the mitochondrial disorder). The psychiatrist must also determine if the symptoms are psychosocial (they are due to the stress of the Mito disorder). It is often unclear if and how the two are related. The more patients that are seen by physicians, the more is learned about the disorders and their relationship to psychiatric disease.

Some of the psychiatric disorders that have a high comorbidity rate with mitochondrial disease are: major depression, psychosis, generalized anxiety disorder, attention deficit hyperactivity disorder, behavioral deregulation secondary to pervasive developmental disorders (this includes autism and autism spectrum disorders), and behavioral deregulation secondary to global developmental delays. Again, it is important for psychiatrists to separate symptoms of a psychiatric disorder from symptoms of the mitochondrial disorder.

The most important factor in treating patients with both mito and psychiatric disease is to do no harm. This seems obvious, but poses very special problems when you consider that a major treatment modality of psychiatric disease is the use of medications. Before resorting to medications to treat psychiatric disorders, Dr. Favero advises seeking other treatments. Psychodynamic therapy can be helpful to help Mito patients work through any internal conflicts. Family therapy can also be useful because many families struggling with a Mito diagnosis suffer from feelings of guilt, frustration, anger, and loneliness. Cognitive-behavioral therapy has also been shown to help Mito patients change with maladaptive thoughts and behaviors that can develop while coping with a Mito diagnosis.

Depression as an example

Major Depression is a common problem for patients with Mitochondrial Disease, and can be used as an example of how psychiatry can help. As with any disease, an accurate diagnosis must be made first. Symptoms for adults with major depression and without a metabolic disorder may include fatigue, decreased concentration, and disturbances in appetite or sleep. However, these symptoms are common in people with mitochondrial disease, and they do not necessarily have major depression. When diagnosing major depression in patients with mitochondrial disease, it is important to focus on the cognitive symptoms such as feelings of hopelessness and worthlessness, low mood, and lack of pleasure. When Mitochondrial Disease is added to the mix of psychiatric symptoms the diagnosis is not so clear cut.

When Major Depression does occur with Mitochondrial Disease, treatment is not necessarily medication. Therapeutic intervention often works first (family or individual therapy). Families of children with Mito are often overprotective, they, as well the patient, may also suffer from high stress and grief. Positive behavioral therapy often helps and can even be life-saving. Advocacy is an important part of this as well. Lifestyle changes such as controlling the temperature of one's environment, decreasing stress, and working in short intervals can improve the patient's condition. Avoiding medications which have severe side effects for mito patients is also a primary concern.

Medications Sometimes medications may be needed (in some cases they may even be life-saving) to help with psychiatric symptoms. These should be chosen and prescribed with great care. The key here is to remember that mito patients have abnormal autonomic regulation; their heart rate, blood pressure and gastrointestinal tract motility may all be affected. It is important to obtain a very good history before proceeding with medications. For example, is there any history of seizures, thyroid dysfunction, or

orthostatic hypotension? A thorough medical history is a must. There is a much higher incidence of side effects from psychiatric medications for mito patients than with the general population.

When treatment is warranted, those medications with the shortest half-life (that is they remain in the body for the shortest period of time) should be used. Among the most used medications, Celexa has the shortest half-life, Zoloft is next and Prozac last, having a longer half-life than the others. Tricyclates can cause the most alterations in the autonomic system and should, therefore, be avoided. MAO Inhibitors are also not recommended due to their side effects. Other medications to avoid are Wellbutrin because it can decrease the threshold for seizures, Effexor because it is contraindicated for children and can cause hypertension, and Rameron because it increases lipids in the blood. Strong medications such as Lithium and thyroid hormones are also dangerous to Mito patients because they can have serious side effects.

Stimulants such as Ritalin may be used for patients with Mito who have been diagnosed with ADHD. When a psychiatrist is prescribing this medication, it is important for him/her to understand the degree and kind of Mito disease and the symptoms which the child has. Proceed carefully and get a clear view of the cause of the cognitive disorder (it may be due to Mito but it may be due to other factors). Get a thorough medical history (neurological/cardiac) because these drugs can cause severe side effects. When effective, these drugs can help because as attention increases, focus improves, stress decreases and this helps mito symptoms as well. Stimulants may also improve stamina in Mito patients.

In regards to bipolar disorder, a caller commented that there are some imaging studies that seem to suggest that the shape of the mitochondria in patients with bipolar disorders is different than those of the general public. The administration of medication will depend very much on the symptoms of the bipolar disorder. Again, the recommendation is to proceed carefully with medications and to carefully weigh risk versus benefit with the use of all drugs. Dr. Favero specifically mentions the use of atypically antipsychotics. These can be dangerous to patients with mitochondrial disease, but the risks of side effects must be compared to the often life-saving benefits of the drug. Supplements can be useful for Mito patients with bipolar disorder, but Dr. Favero states that this should not be the only type of treatment for these patients.

For Mito patients who need a medication for depression, Dr. Favero recommends beginning with one SSRI for a few months. If this does not work, then switch to another. He does not recommend increasing the dose or combining medications. The most important thing to keep in mind when treating Mito patients with psychiatric medications is to try them slowly and to monitor them closely. He also suggests adding more psychiatric interventions like psychotherapy and increased advocacy. Patients with Mitochondrial Disease and psychiatric disease should not be treated in the same manner as the general population. Another important point to remember is the risk vs. benefit of these medications. If someone is in severe psychological distress and is in danger of hurting themselves or others, the risk of side effects of a certain medication

might be worth the life-saving benefits.

Summary

Treating patients with both Mitochondrial Disease and Psychiatric disorders is very new but is increasing at a rapid rate. We are learning new things every day. It is important to have psychiatrists working with the medical doctors as a team. Psychiatrists should take a thorough history and be well educated on the effects of mitochondrial disease on a patient. When prescribing medication, psychiatrists should proceed slowly with caution, and monitor the patient slowly. The main thing to remember when treating these patients is to do no harm, remembering that autonomic regulation is impaired. Psychiatry can help through medication treatment, family support, psychiatric therapy and advocacy.