

New treatment alternatives for Duchenne and Becker muscular dystrophy

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What treatments are available for muscular dystrophy (MD)?

Duchenne and Becker MD are diseases that lead to muscle weakness beginning in childhood. More information about MD can be found on the next page.

There is no cure yet for MD. There are some treatments that can improve symptoms and quality of life. One of the targets for recent new therapies has been to improve muscle strength. For several years prednisone has been used for this purpose. Prednisone is a medication that decreases inflammation in the body. Prednisone has serious and common side effects, however, including weight gain, cataracts, diabetes, high blood pressure, and osteoporosis (weakening of the bones). These side effects limit the use of prednisone to treat MD.

Oral albuterol as an alternative treatment for MD

In this issue of *Neurology*, Fowler and colleagues report the results of a small, pilot study of albuterol to treat children with Duchenne and Becker MD. Albuterol is a medication already approved to treat breathing problems, mostly in patients with asthma. Although this medication is usually used as an

inhaler, this way of taking albuterol has no effect on skeletal muscle. There is an effect on skeletal muscle when a slow-release oral preparation is given. The investigators studied whether treatment with oral albuterol improved the symptoms of MD in these children after taking it for 3 months.

How was the study conducted?

Nine children with Duchenne or Becker MD between the ages of 5 and 9 years took part in the study. Each child was tested for muscle strength and how well their muscles worked before going on study medication. Tests of how well muscles work are called functional muscle tests. These included the time it took to walk or run 30 feet, the time to go up 4 steps, and the time to rise to standing from a lying position. Then each child received either oral albuterol or placebo (sugar pill that looks like albuterol but has no active medication) for 12 weeks and was tested again. This was followed by a 4-week period of taking no study medication. Then the children were given oral albuterol if they got placebo for the first 12 weeks or vice versa for another 12 weeks and were tested again. Neither the children nor the investigators knew when the children were taking albuterol or placebo.

What did the investigators find?

The investigators found that oral albuterol treatment led to an improvement in muscular strength, mostly in the thigh muscles. Not all the muscles showed increased muscle strength. One reason for this might be that some muscles may take up the albuterol better than others. This might lead to more improvement in strength in the muscle that takes up the albuterol the best. Other studies have shown that albuterol may lead to growth of the muscle tissue. This may also lead to improvement in muscle strength. Unfortunately no benefit was found in the muscle function tests. It is possible that more patients need to be studied for a longer period of time to see an improvement in the muscle function.

What do the results of this study mean?

Although the results of this study are promising, larger-scale studies are needed to confirm these findings. No side effects of oral albuterol were reported in this study. If future studies also show that oral albuterol is effective in treating MD, it will be a safe alternative for patients with this disorder.

What are Duchenne and Becker muscular dystrophies (MD)?

MD are a group of muscle diseases that have three features in common: they run in families (are hereditary), they get worse over time, and each causes a characteristic pattern of muscle weakness.

Duchenne and Becker MD cause similar patterns of weakness and disability and are inherited in the same way. Both are due to a problem with the same gene on the X chromosome. This gene normally makes a protein called dystrophin. People with Duchenne and Becker MD have less dystrophin in their muscles than normal. Becker MD is like a milder form of Duchenne MD, with less severe weakness. All forms of MD are considered rare, but Duchenne MD is the most common. Duchenne MD affects approximately 1 boy in every 3,000 and Becker MD occurs in about 1 in 18,000 births.

Who gets Duchenne and Becker MD?

All ethnic groups can get either Duchenne or Becker MD. Both occur mainly in boys (with very few exceptions). Boys have one X-chromosome from their mother and one Y-chromosome from their father. Girls have two X-chromosomes, one from each parent. Because of this, boys are at a greater risk of inheriting disorders caused by damaged genes on the X-chromosome. If a gene on one of a girl's X-chromosomes is damaged, the other one can still work.

How are Duchenne and Becker MD diagnosed?

Duchenne MD is usually diagnosed in boys between the ages of 3 and 7. Parents will often notice that their son is behind other boys their age in developmental mile-

stones. The boy's calves appear to be enlarged (also called pseudohypertrophy), which is another clue that the child's weakness may be due to MD. Becker MD is less severe, and sometimes problems are noticed when the child is older.

The tests available to diagnose Duchenne or Becker MD include a blood test for evidence of muscle damage, electromyography (an examination of the electrical activity generated by muscle when it contracts), a muscle biopsy, and DNA (genetic) testing. For a muscle biopsy, the doctor surgically removes a small sample of muscle and examines it to look for muscle damage. DNA testing (using blood cells or muscle cells) is the best way to get exact genetic information for the diagnosis of Duchenne or Becker MD.

What are the symptoms of Duchenne and Becker MD?

The symptoms and disease course for Duchenne MD are fairly predictable. Becker MD is much more variable. Some people with Becker MD are able to walk only until early adulthood and others to an advanced age. Survival in some is to middle age but others have survived more than 80 years. Some develop heart trouble in early adulthood, others never do.

Boys with Duchenne MD between the ages of 3 and 5 may appear to be clumsy and lose their balance, causing them to fall down a lot during regular activity. Climbing stairs, running, and rising up from the floor become very difficult. By school age, Duchenne MD causes contraction of their Achilles tendons, which forces them to walk either on their toes or on the balls of their feet. This results in a waddling type of walk. In order to keep their balance boys will stick out their bellies and push their shoulders back. This condition is called lordosis.

Between the ages of 7 and 12, most boys with Duchenne MD will lose their ability to walk and depend on a wheelchair for mobility. Throughout the years that follow, they will need help with all activities that call for the use of arms, legs, or trunk muscles. Fatigue is also a problem for boys with Duchenne MD. They struggle with normal levels of activity, but especially when much walking or stair climbing is required.

There is no way to stop Duchenne or Becker MD from progressing once a boy is born with the disorder. However, once a child with Duchenne or Becker MD is born into a family, it is possible to offer prenatal diagnosis in future pregnancies, either for the mother or for other women in her family who may be at risk of being carriers of the damaged X-chromosome.

Genetic tests and genetic counseling

After a boy is diagnosed with Duchenne or Becker MD, it is important to seek genetic advice and appropriate tests for those members of the family who are at risk of being carriers. Genetic testing refers to the analysis of the gene itself and is used to predict if a person is likely to develop a certain disease. A woman's genes can be tested to see if she is a carrier of Duchenne or Becker MD. If she is, doctors may make recommendations about childbearing options.

For more information

American Academy of Neurology Foundation,
www.thebrainmatters.org

Muscular Dystrophy Association,
www.mdausa.org

Muscular Dystrophy Family Foundation, www.mdff.org