Steroids for Duchenne MD: the pros and cons.

For over 20 years boys with Duchenne muscular dystrophy (MD) have been treated with steroids, which is currently the only medication proven to slow the progression of the condition. In Australia, more than 90 percent of boys with Duchenne MD are now treated with steroids but this comes at the price of side-effects which can be very worrying. As a result, it may be difficult for parents to know whether their son should take steroids, and when this treatment should start. In this article we aim to explain what steroids are, what to expect from steroid treatment and suggest topics for discussion with your doctor before and during your son’s steroid treatment.

What are steroids and how do they work?
The steroids used for Duchenne MD are “corticosteroids” (also known as “glucocorticoids”). These are man-made drugs that closely resemble cortisol, a hormone naturally produced by the adrenal glands. Corticosteroids are different from the anabolic steroids used illegally by some athletes. It is not really understood why corticosteroids improve muscle strength in Duchenne MD but it is thought to be due to their anti-inflammatory effects and improvements in muscle regeneration.

Prednisolone and deflazacort are the two types of corticosteroids that are mainly used in Duchenne MD, however deflazacort is not available in all countries. These medications are believed to be equally effective, but prednisone has the advantage of being inexpensive and is available in both tablet and liquid forms. Deflazacort may be preferred for some individuals because it may not cause as much weight gain but it does carry an increased risk of cataracts and fractures.

What are the potential benefits of steroids? What does the research show?
Steroids are recommended in the international standards of care guidelines for Duchenne MD because of their ability to slow the progression of weakness, reduce the development of scoliosis (curvature of the spine) and delay breathing and heart problems.

There is ongoing debate as to the best way to give steroids. However, analysing the clinical records of those who have and haven’t taken steroids has produced a body of evidence that supports their use, and is providing increasing insight into the best time to start steroid therapy.

Recently a database of clinical records in the UK – the North Star database – was used to investigate the long-term effects of steroid use. Information from 396 boys with Duchenne MD taking steroids was used – the largest study of its type ever performed. Some of the boys were taking prednisolone every day while some took it intermittently – 10 days on and 10 days off. Both groups of boys had a decline in their walking ability from the age of seven, but those who were given steroids every day declined more slowly and walked until they were, on average, 14.5 years old. Those taking steroids intermittently walked until they were aged 12, on average. Untreated boys with Duchenne MD are known to stop walking, between the ages of 9 and 10 on average. It has also been suggested that
continuing steroids after becoming a full-time wheelchair user preserves upper body strength, which may allow self-feeding for longer.2

The risk of scoliosis (curvature of the spine) and therefore the need for spinal surgery may also be reduced by steroids. For example, one recent study followed 50 boys with Duchenne MD for 15 years. 92 percent of the boys not on steroids required spinal surgery for scoliosis, whereas only 20 percent of those taking steroids needed this procedure.3 This improvement in spinal health is thought to contribute to the delay in onset of breathing problems in those treated with steroids.

Steroids may also improve heart function. A recent study reported that the average age of cardiomyopathy onset was delayed by about 2 years in those treated with corticosteroids – from 13 to 15 years of age on average.4

The improvement in breathing and heart function would be expected to ultimately lead to improved survival but this hasn’t yet been proven beyond doubt. However, some small studies have indicated increased survival. For example, one Canadian study followed 54 boys with Duchenne MD, 30 of whom started taking daily deflazacort between the ages of seven and 10. It was reported that after 15 years of follow-up, fewer of the boys taking steroids had died (5 percent versus 21 percent).5

It should be noted that there is variability in the response to steroids: for unknown reasons, a proportion of boys have much less benefit than their peers. There is ongoing research to try to understand this, and to develop new steroid medications with fewer side-effects.

**What are the risks?**

The downside of steroid medications, and the reason that people are still very cautious about using them, is their possible side effects. The long-term use of steroids is associated with a number of possible side effects, but not everybody gets them. The most common side-effects reported in Duchenne MD, in the short term, are weight gain and mood changes (irritability and hyperactivity). The face can also become round and puffy, which is referred to as a “Cushingoid appearance”. Excess hair growth and acne can also be a problem for some boys. These side effects can be especially difficult to cope with as boys go into adolescence and their appearance tends to become more important to them, particularly as this is a time when emotional volatility is often an issue regardless of boys’ health status.

Other possible steroid side effects include difficulty sleeping, headaches, mild stomach aches, growth suppression, delayed puberty and cataracts. There can also be a negative impact on the bones. Boys taking corticosteroids have an increased risk of vertebral and limb fractures.

Rare side effects include raised blood pressure, glucose intolerance (diabetes), thinning of the skin, poor wound healing, increased susceptibility to infection, increased sweating and dizziness.

Accurate figures on the frequency of these side effects in Duchenne MD are not available but, in the study mentioned above using the North Star database, about a third of boys on daily prednisolone reported that they had developed Cushingoid appearance, 40 percent had behavioural problems, 14 percent had gastrointestinal symptoms and 22 percent had high blood pressure. This study did not look at boys who were not taking steroids, so it is not known what the baseline rates of these problems are in Duchenne MD.1
In the Canadian study, seven patients out of 37 on deflazacort had vertebral fractures, whereas none of the 42 untreated boys had vertebral fractures. In the same study, treated boys were 10 centimetres shorter on average at 18 years of age and about half developed cataracts (most of which were not severe enough to require treatment).

**Can the side effects be minimised or managed?**

If your son is started on steroids, the team at the neuromuscular clinic will carefully monitor him for possible side effects. If necessary the dose and or type of corticosteroids prescribed for your son can be changed.

Corticosteroids will increase appetite, but weight gain can be minimised by careful monitoring of the diet with help from a dietician. Gastrointestinal problems can be minimised by taking the medicine with meals (a single daily dose with breakfast is usually best), and avoiding non-steroidal anti-inflammatory medicines such as ibuprofen and aspirin. Where required, medication can be prescribed to manage symptoms such as heartburn.

Behavioural problems can be worse in the first six weeks after starting steroids, and may settle down; if not, the team can suggest strategies to try to minimise this problem.

Monitoring of bone health by regular bone density scans and checks of vitamin D and calcium levels is very important. Dietary supplements of Vitamin D and calcium are usually recommended. If problems with growth, cataracts, blood pressure or blood glucose are detected, the specialist will advise on options for management.

If any side effects become intolerable it is advised that the dose of steroid is decreased. Another option is to take them intermittently – for example 10 days on and 10 days off. It has been shown that although taking steroids intermittently is not as effective at maintaining muscle strength as daily treatment, it does still delay heart and breathing problems. Switching to deflazacort is also sometimes better in terms of weight gain and behavioural problems. The team will discuss these options with you if required.

**Do the benefits outweigh the risks?**

This is a difficult question to answer, because the response to steroids differs from person to person. Steroids are recommended as the standard care for boys with Duchenne MD because studies have shown that, in general, they offer significant benefits. The team in the neuromuscular clinic will aim to monitor the benefits and side effects of steroid therapy in your son. If the side effects are outweighing the benefit, the dose can be altered or tapered off completely. This is a decision to be made by you and your son, in discussion with your doctor. It is very important to not suddenly stop taking corticosteroids; their dose needs to be reduced slowly.

**When should steroids be started?**

Steroids are usually started when boys with Duchenne MD are observed to enter a ‘plateau’ phase in their muscle function or earlier. That is, when the motor skills have stopped improving, but have not yet started to decline. This is normally sometime between the ages of four and six. There is recent evidence that starting earlier has a greater long-term effect on boys’ strength and walking abilities.
It is thought that starting steroids later, although not optimal, still has benefits for maintaining muscle strength in the arms, heart and lungs.

**What questions should I ask my doctor?**

This article is not intended to replace discussion with your neurologist. It is important that you ask your doctor all the questions you can think of, and discuss any concerns you have, before making your decision to start steroid therapy.

**Important points to know before starting on steroids**

All routine immunisations should be given before starting corticosteroids (including the varicella vaccine, if your son has not had chicken pox). Children taking corticosteroids should not be given live vaccines such as the MMR (measles, mumps, rubella) vaccine.

You should discuss with your doctor, in advance, what to do if you forget a dose and where to get advice if you’re not sure about his medications. Also be aware that if your son has a sudden stressful event such as illness, an accident or surgery, he may temporarily need a higher dose of steroids. However, it is important you do not change the dose without discussing this with your doctor.

It is recommended that your son wears a MedicAlert bracelet at all times. The bracelet should state that he has Duchenne MD and is taking corticosteroids. Although corticosteroids do not usually interact with other medicines, it is important to check with your pharmacist or doctor before starting any other medications including non-prescription or complementary medicines (herbs, supplements etc).

**Future prospects**

Uncertainties still remain about the different steroid treatment schedules, and at what age to start treatment. To address this, a large international trial is now underway – the ForDMD study. Results from this study are expected within 1-2 years.

Researchers are also searching for better drugs that do not have the side effects of current corticosteroids. Recently a drug called VBP15, which is a synthetic steroid, has been shown in studies in mice to work as well as prednisolone, but with fewer side effects. Clinical trials of VBP15 are being planned.

**Further information**

- The MDA [Duchenne MD factsheet](http://www.mda.org.au/Disorders/Dystrophies/DMD-BMD.asp) contains more information about the condition, including a research summary
- A family guide to the Duchenne MD standards of care is available for download: The [Diagnosis and Management of Duchenne muscular dystrophy- A guide for Families](http://www.treat-nmd.eu/resources/care-overview/dmd-care/family-guide/)

If you have any questions, please contact us:

Email: info@mda.org.au

Phone: (03) 9320 9555
References


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