Steroids in Duchenne dystrophy

We read with interest the recent debate on steroids, growth and motor function decline in Duchenne muscular dystrophy (DMD) [1–3]. The efficacy and safety of growth hormone treatment in 39 ambulant DMD boys with glucocorticoid-induced growth failure was recently evaluated [3]. The authors observed that growth hormone administration led to an increased growth of about 4 cm in the treated as compared to the untreated group, while the motor function decline, during one year of treatment, was similar in both groups.

In 1981, we reported a patient who had DMD and growth hormone (GH) deficiency. This boy remained ambulant until age 19 while his two younger brothers and other relatives who had DMD and normal growth showed a rapid progression of the dystrophic process [4,5]. This observation led us to suggest that GH inhibition could be beneficial and slow down the progression of muscle decline [6]. This was attempted in a pair of monozygotic DMD twins who were treated with mazindol, an “anorexigenic” drug, which supposedly could inhibit GH release. One twin received the drug, while the other took a placebo in double blind test. After one year, the twin who received the drug had grown only 0.5 cm and had a significantly better motor performance than his brother under placebo who had grown 3 cm during the same period. However, unfortunately the drug was not effective in inhibiting GH release for a longer period of time and, therefore, the hypothesis that GH inhibition could slow down the progression of the dystrophic process could not be confirmed [7]. We also analyzed the relation between height and the course of DMD in a cohort of 92 patients [8] which suggested an inverse correlation between height and motor performance but in another subsequent study we also observed that GH release is not always directly correlated with height [9].

It is important to point out that, in addition to animal models, another rare patient with DMD and GH deficiency was reported after wards by another group [10]. According to the authors, this boy had no clinical evidence of muscle weakness before initiation of GH replacement therapy. After growth hormone administration, he developed muscular dystrophy which led the authors to suggest that patients should be tested for muscular dystrophy before taking GH.

More recently we ascertained a 9-year-old BMD patient (with an “in frame” 45–47 deletion) who was also treated with GH for 18 months due to severe growth delay. According to his mother this boy had no signs of muscle weakness before GH administration. These observations reinforce our suggestion that growth hormone release may be detrimental and accelerate loss of motor ability in DMD patients.

Since steroid administration is now routinely used as a treatment for DMD, complaints about delayed growth are not rare during patients’ follow-up. Our advice has been against growth hormone administration. The recent observation from Rutter et al. [3] showing that with the exception of 3 patients there were no detrimental effects in DMD patients with improved growth should be confirmed for a longer period of time. While this is still an open question, we agree with Prof. Dubowitz [1] that the benefit and potential side effects of different approaches should be extensively discussed with patients and parents and in particular the possibility that growth hormone administration may accelerate muscle decline. Finally, although we understand that short stature may cause a negative body image, it might be better to be of shorter stature and still ambulant than taller but confined earlier to a wheelchair.

References


Mayana Zatz*
Rita C.M. Pavanello
Human Genome and Stem-Cell Research Center, Institute of Biosciences, University of São Paulo, São Paulo, Brazil
* Tel.: +55 11 30917581.
E-mail address: mayazatz@usp.br (M. Zatz)