MR supports therapeutic effects of corticosteroids in 5-7 year old boys with DMD

Isihu Arpan1, Rebecca Willoc1, Stevan Forbes1, Donovan Lott1, Claudia Sene1, William Tripp1, Michael Daniels2, Barry Byrne3, Erika Finanger4, Richard Finkel1, Barry Russman1, Gihan Tennekoon1, Dah-Jyuu Wang4, Glenn Walter5, H. Lee Sweeney6, and Krista Vandenbome1


Target Audience: This study will benefit those interested in implementing magnetic resonance imaging (MRI) and spectroscopy (MRS) for monitoring skeletal muscle response to disease progression as well as therapeutic interventions in muscular dystrophies or other neuromuscular disorders characterized by muscle damage, edema, inflammation or fatty tissue infiltration.

Introduction: Duchenne muscular dystrophy (DMD) is one of the most debilitating forms of the muscular dystrophy. Currently, there is no cure for the disease. Glucocorticosteroids (Prednisolone and Deflazacort) have been reported to slow down the disease progression in DMD1-4. However, the mechanism by which corticosteroids preserve muscle function in DMD is not fully understood. Magnetic resonance imaging (MRI) and spectroscopy (MRS) can provide information about skeletal muscle pathologies that are associated with the disease process of DMD, such as inflammation and fatty tissue infiltration5-7. Therefore, the purpose of this study was to utilize MR measures to study the effects of corticosteroid treatment on lower extremity muscles of 5-7 year old boys with DMD.

Methods: MR data were acquired from 15 young boys with DMD treated with corticosteroids (mean age: 6.1±0.1 yrs) and 15 age-matched corticosteroid-naive boys (mean age: 6.1±0.1 yrs) using 3T MR systems at three institutions. T2-weighted spin echo (SE) images [4-8 axial slices, repetition time (TR): 3 s, 16 echo times (TE’s): 20-320 ms, slice thickness: 7 mm, slice gap: 3.5 mm] were acquired on the lower leg and thigh. In addition, two sets of unsuppressed localized 1H MRS scans were acquired. To measure the relative intramuscular fat fraction a single voxel STEAM spectra (Sol) and vastus lateralis (VL) muscles. In addition, spectroscopic relaxometry sequences using 1H-MRS STEAM were implemented to quantify 1H-O T2 in the Sol (TR: 9 s; 16 TE’s: 11-288 ms, NA: 4) and VL (TR: 9 s; 4 TE’s: 11-252 ms, NA: 4). Finally, functional performance of all boys was assessed using a timed 6-minute walk test (6MWT). In addition to cross-sectional comparisons at baseline, longitudinal analysis of the change in fat fraction over one year was measured in a subset of DMD boys in both the corticosteroid treatment group and corticosteroid-naive group.

Results and Discussion: MRI-T2 values were significantly lower in the lower leg muscles of boys on corticosteroid treatment compared to corticosteroid-naive boys (Sol: 36.6±0.7ms vs. 45.6±0.7ms; Medial gastronemius (MG): 37.9±0.4ms vs. 46.6±1.1ms; Peroneals (Per): 37.8±0.1ms vs. 43.8±1.0ms). MRS-T2 values in Sol and VL muscles of the treatment group were also lower (p≤0.05) and the Biceps femoris long head muscles (BFl): 39.8±0.9ms vs. 46.6±1.1ms, p≤0.05). Similar results were observed in VL (39.6±0.7ms vs. 46.3±1.5ms, p≤0.05) and the Biceps femoris long head muscles (BFl) in the treatment group (39.8±0.9ms vs. 46.6±1.1ms, p≤0.05), indicating less inflammation/damage in the muscles of boys on corticosteroid therapy (Fig: A). Therefore, the results of this study support the proposed role of corticosteroids in reducing inflammatory processes in skeletal muscles in DMD. In addition, the intramuscular fat fraction was significantly lower (p≤0.05) in the muscles of boys on corticosteroid treatment compared to corticosteroid-naive boys over one year (Fig: B). While both MRI and MRS showed positive effects of corticosteroids on skeletal muscles of 5-7 years old boys with DMD, no significant difference could be detected in the 6MWT across the groups (Corticosteroid-naive: 348.0±15.7 and Corticosteroid: 367.4±15.5, p=0.4). Although the 6MWT has been established as a clinically meaningful outcome measure in DMD, these data indicate that it may be less sensitive in monitoring muscle response to disease progression or therapies, especially in younger boys with DMD.

Conclusion: MRI/MRS results showed that T2 values and fat fraction were significantly lower in thigh and leg muscles of boys with DMD in the treatment group; suggesting reduced inflammation/damage and fatigue in corticosteroid treatment. These findings support the therapeutic effects of corticosteroids on muscle quality in 5-7 year old boys with DMD. In addition, these results demonstrate the potential of MRI and MRS to monitor muscle response to anti-inflammatory and other potential therapeutic interventions in young boys with DMD.

Figure: An example SE image of the lower leg with voxel placement in the soleus (Sol) muscle is depicted with the corresponding spectra acquired during the spectroscopic relaxometry scan (A). Cross-sectional comparisons of MRI T2 (B) and fat fraction (C) among boys on corticosteroid (CS) treatment and corticosteroid-naive (CS-naive) boys and the longitudinal changes in fat fraction over one year in the Sol and vastus lateralis (VL) muscles of boys in both groups are shown (D). Values are represented as mean ± SE; ** p≤0.01 & * p≤0.05.


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