The Role of Rehabilitation in Preventing Steroid Induced Myopathy

David Nieves, MD, Jason Lam DO

Department of Physical Medicine & Rehabilitation at Zucker School of Medicine at Hofstra/Northwelll

INTRODUCTION

Steroid induced myopathy is a condition that was first identified when physicians began to use glucocorticoids as treatment options in the 1950s. The effects of the corticosteroids are well known in the chronic phase, but much fewer cases have been recognized in the more acute phase. Acute steroid myopathy is usually seen with critically ill patients who require high-dose intravenous corticosteroids to go along with ventilatory support. However, there have been cases in which an “acute steroid myopathy” can occur in patients receiving oral corticosteroids in moderate doses for outpatient treatment.[1]

Glucocorticoids directly catabolize skeletal muscle by targeting muscle proteins for degradation through the ubiquitin-proteasome pathway in order to provide amino acids to act as a substrate for gluconeogenesis. Corticosteroids suppress Akt1, an intracellular signaling molecule with protein kinase activity, which leads to increased levels of the ubiquitin-ligase atrogin-1 (MAFbx), which targets muscle proteins for degradation.[2,3] Glucocorticoids may also interfere with muscle differentiation by accelerating the degradation of MyoD, a major transcriptional switch for muscle development and regeneration.[4] MyoD is required for self-proliferation of skeletal muscle satellite cells, which in turn allows for normal muscle structure and function. The combined effect of these interactions, as well as other cellular processes, causes atrophy, seen on a macroscopic level as muscle weakness and wasting.

When prescribers see a patient begin to develop steroid induced weakness, usually diagnosed by manual muscle testing, the first step is to reduce the corticosteroid dose.[1] Muscle strength normally starts to improve by three to four weeks after the reduction, and if the corticosteroids are tapered completely off, strength will return in full. Some patients, however, will require a little extra assistance regaining their strength, mobility, and independence, and will benefit from a short stay in an acute inpatient rehabilitation facility.

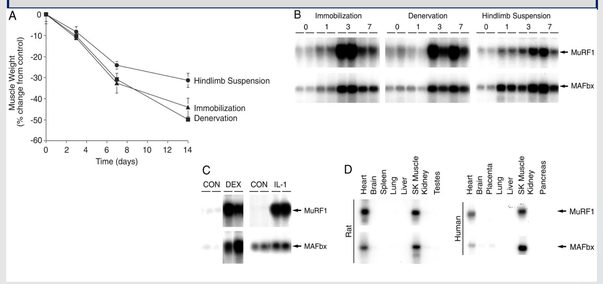
PATIENT PRESENTATION

A 61 year old female presented to the Emergency Department with progressive lower extremity weakness over the previous month. Patient had a history of Breast Cancer stage I/II in 2006, status post lumpectomy, radiation therapy, and tamoxifen for three years, Primary Lung Cancer, status post right VATS and right upper lobe wedge resection, and Nasopharyngeal Cancer, status post resection of left Meckel’s cave trigeminal schwannoma, 3 cycles of high dose cisplatin and gemcitabine from June -August 2019, current treatment with Nivolumab every four weeks, and gamma knife radiation on 4/2/20, three weeks prior to admission. Patient stated that she was taking steroids since the gamma knife procedure. Initial workup was to rule out cord compression, and MRI was negative for any cord compression, though it did show bony metastases. Initial physical therapy evaluation showed manual muscle testing of 3+/5 strength in bilateral upper extremities, 3/5 in the right lower extremity, and 3-/5 in the left lower extremity with impairments in strength and balance. Patient was ambulating with contact guard and minimum assist of one person for 40 feet with a rolling walker. Patient was started on a Decadron taper and was recommended for acute inpatient rehabilitation.

When the patient arrived at Glen Cove Hospital, her first physical exam was notable for strength in her bilateral upper extremities of 5/5, and decreased strength in her proximal lower extremities. Her left lower extremity was 3/5 strength for hip abduction and hip flexion, 4/5 for hip adduction and knee extension, and 5/5 for dorsiflexion and plantarflexion. Her right lower extremity was 4/5 for hip flexion and 5/5 for knee extension, dorsiflexion, and plantarflexion. Her sensation was intact to light touch in all four extremities, and her reflexes were normal. During her stay of 13 days, patient received two hours of physical therapy and one hour of occupational therapy daily. Patient completed her Decadron taper and made gains in therapy in regards to her strength and balance. She was able to ambulate with modified independence with a rolling walker and she was discharged home, where she lived alone. Upon discharge, patient’s proximal lower extremity strength improved to 4/5 bilaterally on manual motor testing and she will continue to receive physical therapy through home care and will follow up as an outpatient with physiatry.

DISCUSSION

In patients undergoing high dose corticosteroid therapy, steroid induced myopathy can lead to adverse effects, such as weakness and falls, which in turn can lead to an increased risk of brain injury, acute fractures and overall deconditioning. Exercise while undergoing corticosteroid treatment can be used as a preventative measure for these adverse effects.[5] In a rodent-based study by Uchikawa, Hase, Masakado, and Liu, muscle fibers were evaluated after receiving steroids alone, steroids with high intensity exercising, and steroids with moderate intensity exercising.[6] Their results showed that high-intensity exercise when combined with steroid use leads to muscle fiber atrophy and changes in the fiber distribution compared to moderate-intensity exercise. This shows that while over-exertion of muscles while being treated with corticosteroids may be detrimental, a regulated physical therapy regimen of moderately intense exercises may be beneficial to preventing muscle atrophy and weakness.



(A) Three different models of skeletal muscle atrophy. (B) Northern blots showing the effect of atrophy on MuRF1 and MAFbx transcripts (C) Northern blots showing the effect of dexamethasone (DEX) and IL-1 on expression ofMuRF1 and MAFbx. (D) Tissue-specific expression of MuRF1 and MAFbx. SK, skeletal.[3]

TABLE 1 Distribution of muscle fiber types in the soleus muscle

	C	S	SE15	SE30
Type I	86.5 ± 0.7**	74.3 ± 2.6**	83.5 ± 5.3*	77.7 ± 2.2*
Type IIc	2.9 ± 0.9***	12.6 ± 5.5*	9.2 ± 4.6*	11.9 ± 2.8*
Type IIa	10.6 ± 0.7	13.1 ± 7.8	7.3 ± 5.6	10.4 ± 2.7

* C vs. S and SE30, S vs. SE15: $P < 0.05$; ** C vs. S, SE15, and SE30: $P < 0.05$. Mean ± SD (%).

Distribution of muscle fibers types in the soleus muscle.[6]

CONCLUSION

Many patients require corticosteroid therapy as an important piece of their treatment plan. However, steroids are not without side effects, including the risk of muscle atrophy. Because this atrophy tends to occur in the proximal lower extremity muscles, falling and an inability to ambulate can occur.
As physiatrists, it may be beneficial to recommend a course of outpatient or home care physical therapy to patients who are starting treatment with steroids. It is essential that when therapy is initiated, the patient, therapist, and physician work together to create a program that allows for moderate-intensity exercise, as this level of intensity will lead to muscle hypertrophy rather than atrophy. Another consideration to exercise therapy is that patients who are requiring high dose corticosteroid treatment may have a more complex disease process that could leave them weakened and deconditioned regardless of steroid use. These patients may benefit from a stay in an acute inpatient rehabilitation center where they would be able to receive this physical therapy while under the care of a physician who is able to monitor their disease progression and their tolerance to initiating an exercise program.

REFERENCES

1. M Haran, A Schattner, N Kozak, A Mate, A Berrebi, L Shvidel, Acute steroid myopathy: a highly overlooked entity, *QJM: An International Journal of Medicine*, Volume 111, Issue 5, May 2018, Pages 307–311, https://doi.org/10.1093/qjmed/hcy031
2. Sandri M, Sandri C, Gilbert A, et al. Foxo transcription factors induce the atrophy-related ubiquitin ligase atrogin-1 and cause skeletal muscle atrophy. *Cell*. 2004;117(3):399-412. doi:10.1016/s0092-8674(04)00400-3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3619734/
3. Bodine SC, Latres E, Baumhueter S, et al. Identification of Ubiquitin Ligases Required for Skeletal Muscle Atrophy. Science. https://science.sciencemag.org/content/294/5547/1704. Published November 23, 2001.
4. Sun L, Trausch-Azar JS, Muglia LJ, Schwartz AL. Glucocorticoids differentially regulate degradation of MyoD and Id1 by N-terminal ubiquitination to promote muscle protein catabolism. *Proc Natl Acad Sci U S A*. 2008;105(9):3339-3344. doi:10.1073/pnas.0800165105. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2265166/
5. Nakago K, Senda M, Touno M, Takahara Y, Inoue H. Influence of exercise on muscle fibers in rats with steroid myopathy. *Acta Med Okayama*. 1999;53(6):265-270. doi:10.18926/AMO/31621. https://pubmed.ncbi.nlm.nih.gov/10631381/
6. Uchikawa, Ken MD; Takahashi, Hidetoshi MD, PhD; Hase, Kimitaka MD, PhD; Masakado, Yoshihisa MD, PhD; Liu, Meigen MD, PhD Strenuous Exercise-Induced Alterations of Muscle Fiber Cross-Sectional Area and Fiber-Type Distribution in Steroid Myopathy Rats, American Journal of Physical Medicine & Rehabilitation: February 2008 - Volume 87 - Issue 2 - p 126-133 doi: 10.1097/PHM.0b013e31815869d0. https://journals.lww.com/ajpmr/pages/articleviewer.aspx?year=2008&issue=02000&article=00005&type=Fulltext