0363-5465/99/2727-0002$02.00/0
THE AMERICAN JOURNAL OF SPORTS MEDICINE, Vol. 27, No. 1
© 1999 American Orthopaedic Society for Sports Medicine

The Effect of Anabolic Steroids and Corticosteroids on Healing of Muscle Contusion Injury*

John M. Beiner, MD, Peter Jokl, MD, Jacek Cholewicki,† PhD, and Manohar M. Panjabi, DrTech, PhD

From Yale University School of Medicine, Department of Orthopaedics and Rehabilitation, New Haven, Connecticut

ABSTRACT

The effect of an anabolic steroid (nandrolone decanoate, 20 mg/kg) and a corticosteroid (methylprednisolone acetate, 25 mg/kg) on healing muscle injured with a drop-mass technique in a reproducible muscle contusion injury model in the rat was studied. Healing was determined by measuring active contractile tension in each muscle and histologic analysis. At day 2, the corticosteroid group showed significant improvement in both twitch and tetanic strength relative to the controls. At day 7, this effect was reversed and the corticosteroid muscles were significantly weaker than the control muscles, but there was still no significant effect seen in the anabolic steroid group. At day 14, the corticosteroid muscles were totally degenerated, with disorganized muscle fiber architecture. The anabolic steroid muscles were significantly stronger in twitch, and a similar trend was seen in tetanus relative to control muscles. The results indicate that in an animal model corticosteroids may be beneficial in the short term, but they cause irreversible damage to healing muscle in the long term, including disordered fiber structure and a marked diminution in force-generating capacity. Anabolic steroids may aid in the healing of muscle contusion injury to speed the recovery of force-generating capacity. Although anabolic steroids are considered renegade drugs, they may have an ethical clinical application to aid healing in severe muscle contusion injury, and their use in the treatment of muscle injuries warrants further research.

Contusion and strain injuries make up approximately 90% of all sports-related injuries.[1,2,4,7] Other than strain injuries, contusion caused by impact with a blunt, nonpenetrating object is the most frequent type of muscle injury.[15] At a microstructural level, the injury involves capillary rupture and infiltrative bleeding, edema, and inflammation. This leads to hematoma formation and can cause compartment syndrome in areas where volumes are limited by fascial planes. Symptoms of a contusion injury are often nonspecific and include soreness, pain with active and passive motion, and limited range of motion. Without a straightforward history of an impact to the area, the diagnosis becomes one of exclusion. Many contusion injuries go unreported and untreated, and, as a result of these difficulties in diagnosis and evaluation, no universally accepted treatment modalities have been developed. Most clinicians agree with the RICE principle (rest, immobilization, cold, and elevation), at least in the short term, but they differ as to the best long-term treatment.

Jackson and Feagin[16] studied quadriceps muscle contusions at West Point and introduced an initial classification scheme based on range of motion and a rationale for treatment with early extension immobilization followed by extension exercises. A later study from the same institution modified the treatment regimen to immobilize in flexion with early passive pain-free motion emphasizing flexion.[28] Jarvinen and colleagues[17–19,21] developed a rat model of muscle contusion injury using a spring-loaded hammer and compared the effects of mobilization and immobilization on the healing process. They found that early mobilization increased the tensile strength of the muscle compared with similarly injured muscles immobilized in a plaster cast. Evidence supporting the use of other treatment modalities is scarce, however. Nonsteroidal antiinflammatory drugs are often used in the clinical setting, although data regarding their short- and long-term benefits are conflicting.[6,20,24] Despite the fact that

* Presented at the interim meeting of the AOSSM, San Francisco, California, February 1997.
† Address correspondence and reprint requests to Jacek Cholewicki, PhD, Yale University School of Medicine, Department of Orthopaedics and Rehabilitation, POB 208071, New Haven, CT 06520-8071.
No author or related institution has received any financial benefit from research in this study.

corticosteroids have repeatedly been shown to be catabolic and inhibit the healing process,[8,9,13,20,23,25–27,31–33] they continue to be used clinically to treat muscle contusion injuries and are injected into the site of injury to relieve pain and expedite a player's return to active status.

Anabolic steroids have often been contrasted with corticosteroids in their effects on muscle tissue, with widely conflicting reports as to their advantages and disadvantages. These steroids have been shown to promote muscle growth and regeneration in some circumstances.[10,12,14,22,29,31,33–36] In addition to their more traditional role in the treatment of anemia and hypogonadism in male patients, they have been used to treat various conditions that represent the "catabolic state," including hip fractures, burns, and old age. Despite the institution of more and more stringent rules and tests in many organized competitions, anabolic steroids are used illicitly in a wide variety of competitive sports, with perhaps the most publicized being track and field, football, body building, and power lifting. In 1984, Haupt and Rovere[11] reviewed the literature on human anabolic steroid use. They concluded that anabolic steroids can consistently enhance athletic performance if the following conditions are met: the subject has undergone previous training and takes in a high-protein diet, and "performance" is measured by single-repetition maximal strength tests. In other studies, benefits of anabolic steroids have been found to be activity dependent, muscle fiber type dependent, and diet dependent. The mechanism and overall effects on muscle tissue are still debated.

We hypothesized that an anabolic steroid may be useful in the treatment of contusion injuries because of the drug's effects on nitrogen and protein balance and on stimulation of cell synthesis. We also hypothesized that a catabolic steroid, with opposite effects on the above processes, would, in contrast, be detrimental to healing. The purpose of this study was to examine the effects of nandrolone decanoate, an anabolic steroid, and of methylprednisolone acetate, a catabolic steroid, on the healing of muscle contusion injuries as measured by the recovery of force-generating capacity. Our laboratory has developed a model that, in contrast to other animal models, can cause a standard, reproducible contusion injury to the gastrocnemius muscle in rats, characterized in terms of force, displacement, energy, and impulse.[3] We compared the injured muscle to the contralateral, uninjured muscle, as well as to injured muscles in control animals given saline injections.

MATERIALS AND METHODS

All experimental procedures and pharmacologic agents were approved by the Yale Animal Care and Use Committee under Protocol #6566.

Impact Parameters

Forty-five skeletally mature male Wistar rats, weighing 250 to 300 g, were anesthetized with ketamine and xylazine and secured to a holding apparatus. The impact apparatus (Fig. 1) and method of testing have been described in a previous publication.[3] Briefly, one hindlimb was secured to the rigid impacting base containing a load cell to measure the force of the impact. The ankle was secured at 90° of flexion, and the knee was extended. The impactor surface was a sphere (diameter, 9 mm) that directly contacted the skin over the posterior gastrocnemius muscle and was connected to a linear variable differential transducer to measure the displacement of each impact. The shape and size of the impactor surface were designed to simulate a corresponding injury in humans from a ball or helmet. Platinum stimulating electrodes were placed subcutaneously on either side of the gastrocnemius muscle of the leg to be injured. While the muscle was contracted to tetanus, using a supramaximal voltage and frequency, a mass of 171 g was dropped from a height of 102 cm onto the top of the impactor, causing the injury. Voltage and frequency of stimulation were chosen based on force-frequency and force-voltage curves established with our preparation before this study and were adjusted to produce maximal tetanic contraction without damaging the muscle. Previous studies in this laboratory have shown that impact on a contracted muscle in this position gives the most reliable and reproducible injury, consisting of a partial-thickness crush injury to the gastrocnemius muscle (unpublished data). The load-time and displacement-

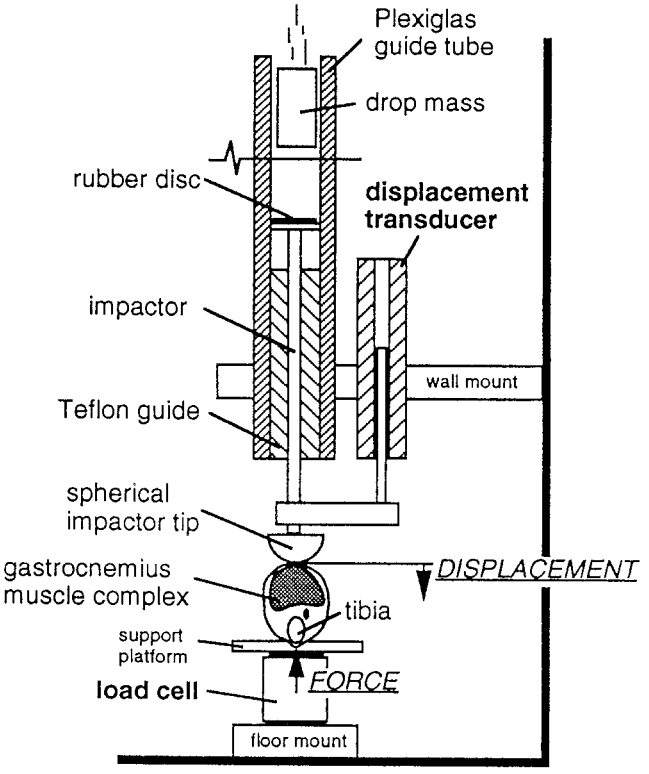

Figure 1. Schematic of impact apparatus, looking at a cross-section of the leg (Reprinted from *Journal of Biomechanics*, Volume 29, J.J. Crisco, K. D. Hentel, W. O. Jackson, et al., Maximal Contraction Lessens Impact Response in a Muscle Contusion Model. pp 1291–1296, 1996, with permission from Elsevier Science.)

time data of each impact were collected, graphed, and analyzed by computer, with a sampling frequency of 10,000 Hz (Fig. 2). The contralateral leg of each animal was left uninjured.

Experimental Protocol

After the impacts, the animals were sequentially assigned to one of three groups: 1) control, 2) anabolic steroid, and 3) corticosteroid. Control rats received an injection of saline, divided into two parts and given intramuscularly into the gluteous maximus on each side to cause systemic absorption. All rats in the anabolic group received a one-time dose of 20 mg/kg nandrolone decanoate (Deca-Durabolin, Organon, West Orange, New Jersey), a long-acting anabolic steroid, divided and injected as above. Rats in the corticosteroid group received a one-time dose of 25 mg/kg methylprednisolone acetate (Depo-Medrol, Upjohn, Kalamazoo, Michigan), a long-acting antiinflammatory steroid, divided and injected as above. Dosages were determined from a literature review of all studies using corticosteroids or anabolic steroids in small rodents, after correcting for the relative potencies of each drug and for the depot intramuscular form. Because the metabolism of the rat is so much faster than that of humans, any local dose of steroid rapidly becomes systemic and, as anabolic steroids are injected this way in humans anyway, we elected to give all treatments as bilateral intramuscular injections away from the site of injury.

Testing Protocol

Five animals from each group were tested at intervals of 2, 7, and 14 days. The force-generating capacity of the muscles under study was measured as twitch strength and tetanic strength. The methods of contractile testing have been described in a previous publication.[3] Briefly, after administration of anesthesia, the gastrocnemius muscle of each limb was isolated and connected to a force transducer, leaving its neuromuscular supply and overlying skin intact. The sciatic nerve was isolated and transected proximally. Stimulation of the distal nerve was accomplished in a bipolar mode, with one electrode attached to the sciatic nerve and one inserted into the distal muscle belly. The muscle was then stimulated (5 V, 0.05 msec duration), using a Grass S44 stimulator (Grass Instruments, Quincy, Massachusetts), at different lengths (spaced 0.025 inches apart) to find the optimum length (L_o) of the muscle; that is, the length at which maximal twitch and tetanic force are generated. Supramaximal voltage and frequency were used to assure complete twitch recruitment and tetanic fusion, generating maximal tetanic force (P_{max}) in each case. The Achilles tendon was kept moist with normal saline and paraffin oil. The temperature of the preparation, as monitored by a rectal probe, was maintained constant at the physiologic level of 38.1° ± 1.50°C with the use of an ambient heat lamp. The preparation was found to be stable over a period of several hours, much longer than was necessary to test each animal. The tester was blind as to which leg was injured in each rat.

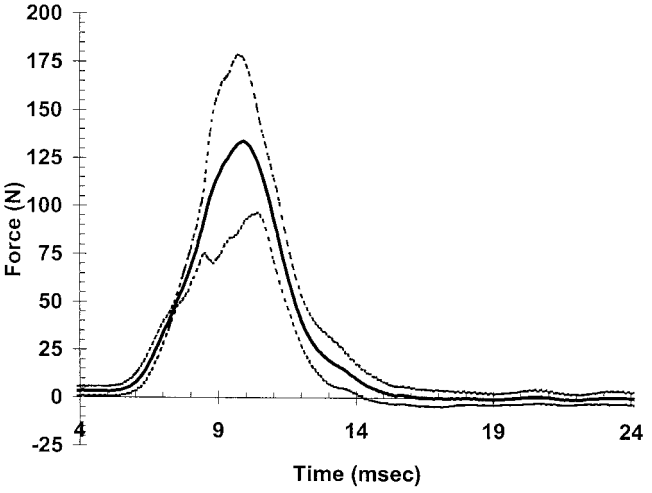

Figure 2. Composite of all impacts, irrespective of treatment group. The solid line represents the average force and dotted lines represent one standard deviation above and below average.

Histologic Preparation

A representative sample muscle from each group was isolated and preserved in 3% formalin for 2 days. The samples were then divided into three sections corresponding to three zones of injury: proximal, middle, and distal, and embedded into paraffin. Slices were taken of each of these blocks to ensure that we had the injury site represented in our histologic analysis, and sections were stained with hematoxylin and eosin.

Statistical Analysis

The three-way analysis of variance (ANOVA) was used to evaluate the recovery of muscle force-generating capacity. Treatment (control, corticosteroids, anabolic steroids), day (2, 7, 14), and injury status (injured versus uninjured leg) constituted the three factors. Statistical significance level was set at $P = 0.05$. Separate analyses for the two outcome parameters (twitch and tetanus) were performed. The Fisher's least-significant-difference test was used to evaluate the selected comparisons. Group averages are expressed as means plus or minus the standard deviations of the means to describe variability within our sample population.

RESULTS

The results of a three-way ANOVA returned significant main effects of treatment, day, and injury status on muscle strength recovery in twitch and tetanus. Significant interaction between the treatment and day was also found.

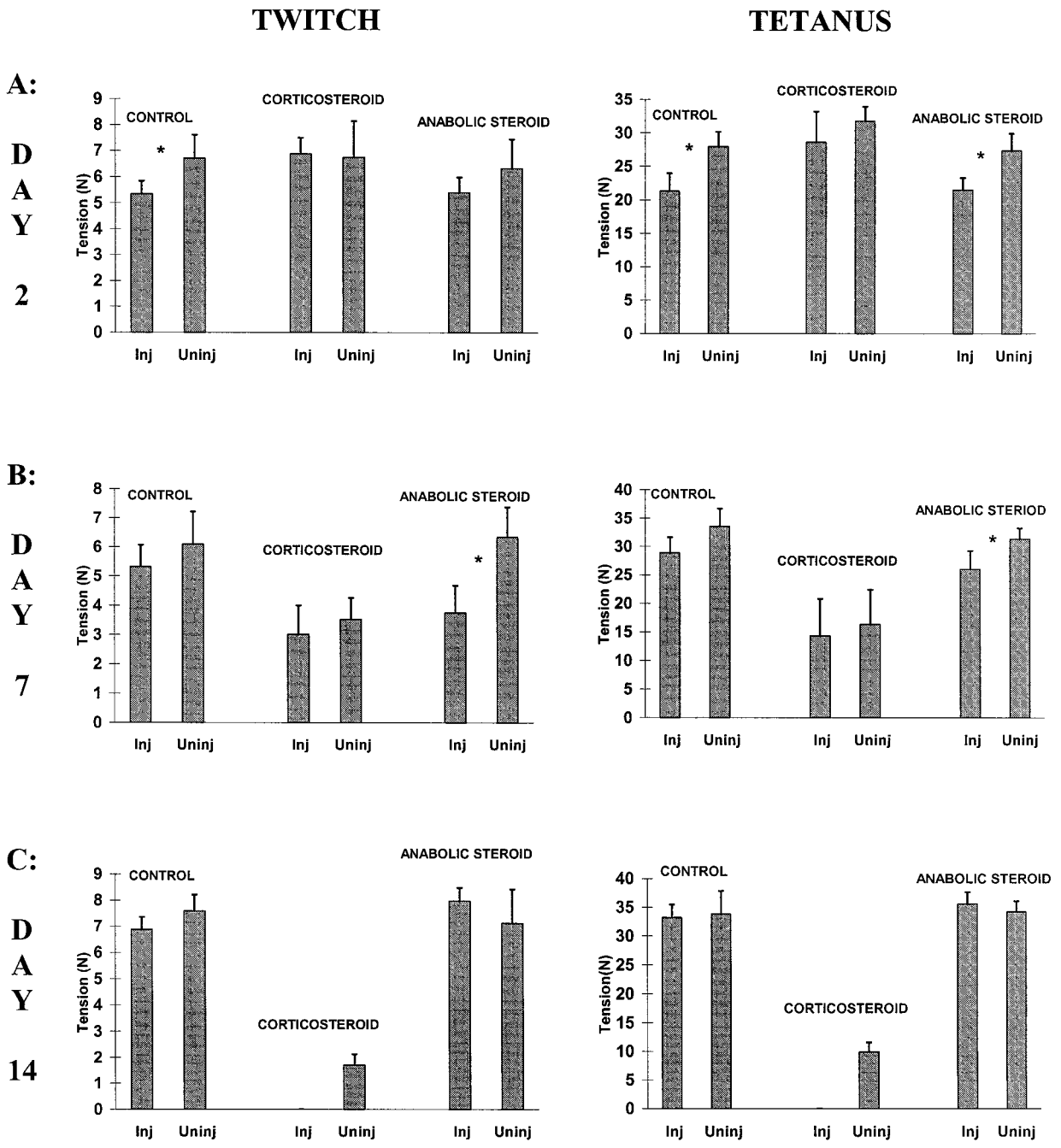

Figure 3. Comparison of maximal force-generating capacity (tension, in newtons) in twitch and in tetanus between the injured legs (Inj) and the contralateral control uninjured legs (Uninj) within each treatment group at day 2 (A), day 7 (B), and day 14 (C). *, $P < 0.05$ between injured and uninjured legs.

Body Weight

Control animals gained 44 g on average by day 7, and 88 g by day 14. Animals in the anabolic steroid group also gained weight: 63 g at day 7 and 109 g at day 14. These weight gains were not statistically significant. In the corticosteroid group, the animals lost weight: −69 g of total body weight by day 7, and −104 g by day 14. This loss was significant when compared with the control animals. One animal in the corticosteroid group died at day 13 and was eliminated from the study.

Muscle Healing Relative to the Uninjured Leg

Twitch and tetanic tension measurements for all groups at three time points were collected, and data are reported as the average (plus or minus one standard deviation).

Day 2. In control animals on day 2, the injured muscles were significantly weaker than the uninjured muscles in twitch and in tetanus (Fig. 3A). Within the anabolic steroid group, the injured muscles were significantly weaker than the uninjured muscles in tetanus, but they were not significantly weaker in twitch. In the corticosteroid group, the injured muscles at day 2 were not significantly weaker in either twitch or tetanus.

Day 7. In all groups at day 7, the injured muscles were not found to be significantly weaker or stronger than the uninjured muscles (Fig. 3B).

Day 14. In control group animals, all differences between strength in injured and uninjured muscles remained nonsignificant (Fig. 3C). Strength was similar in twitch and in tetanus. In the anabolic steroid group, the injured muscles were in all cases stronger at day 14 than the uninjured muscles, although this difference did not reach statistical significance in either twitch or tetanus. In the animals given corticosteroid, the injured muscles had atrophied and degenerated to such an extent that testing was unreliable. Several legs had nonhealed, angulated fractures of the tibia, causing the muscle fibers to be disorganized. Accordingly, no data are reported for injured muscles at day 14 in the corticosteroid group. Strength in the uninjured muscles in the corticosteroid group was markedly diminished in twitch (1.7 N [0.4]) and in tetanus (10.0 N [1.6]).

Comparison of Muscle Healing Between Treatment Groups

Day 2. At 2 days, there was no significant difference between injured muscles in the control group and injured muscles in the anabolic steroid group in either twitch or tetanus (Fig. 3A). In the animals given corticosteroids, however, the injured muscles were significantly stronger than the injured muscles in the control group in twitch (6.9 N [0.6] versus 5.4 N [0.5]) and in tetanus (28.6 N [4.6] versus 21.3 N [2.6]). This increased strength of corticosteroid muscles at day 2 was also true for uninjured muscles stimulated to tetanic contraction; they were statistically stronger than the uninjured muscles in the control group (31.8 N [2.2] versus 28.0 N [2.2]).

Day 7. After 1 week there was again no significant difference between the anabolic and control groups in terms of twitch and tetanic contraction, in either injured or uninjured muscles (Fig. 3B). In the corticosteroid group, however, we observed a marked decrease in force-generating capacity relative to control muscles. Injured muscles were significantly weaker in twitch (3.0 N [1.0] versus 5.3 N [0.8]) and in tetanus (14.3 N [6.5] versus 28.9 N [2.8]). The uninjured muscles in the corticosteroid group were also significantly weaker than uninjured muscles in the control animals in twitch and in tetanus.

Day 14. At 14 days, comparison between the control and anabolic groups revealed that the injured muscles in the anabolic group were significantly stronger than injured muscles in the control group in twitch force (8.0 N [0.5] versus 6.9 N [0.5]), with a similar trend in tetanus (35.6 N [2.1] versus 33.2 N [2.2]) ($P = 0.167$) (Fig. 3C). There was no significant difference between uninjured muscles in the anabolic versus control groups. Comparison between the corticosteroid group and control group was again impossible because of our inability to test the injured muscles in the corticosteroid group at day 14. The uninjured corticosteroid muscles were significantly weaker than uninjured control muscles both in twitch and in tetanus.

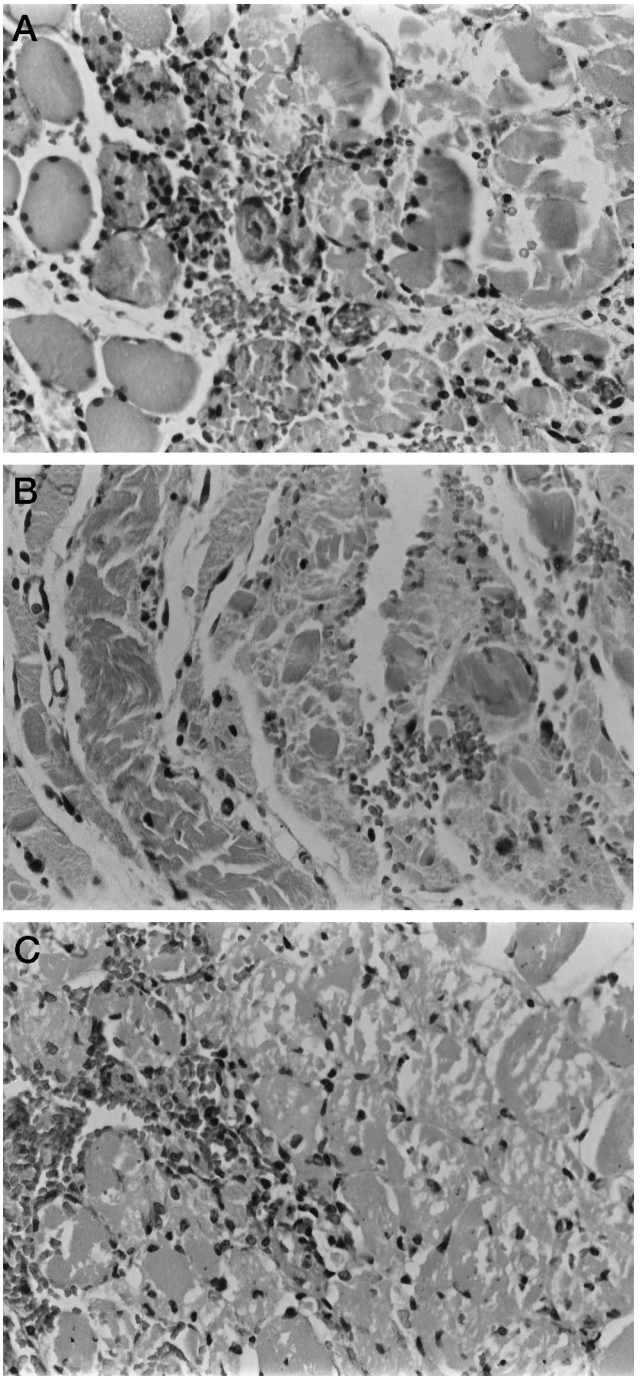

Figure 4. Light microscope photographs of hematoxylin and eosin-stained sections of injured muscle tissue from the control group (A), corticosteroid group (B), and anabolic steroid group (C) at day 2. (original magnification, ×20)

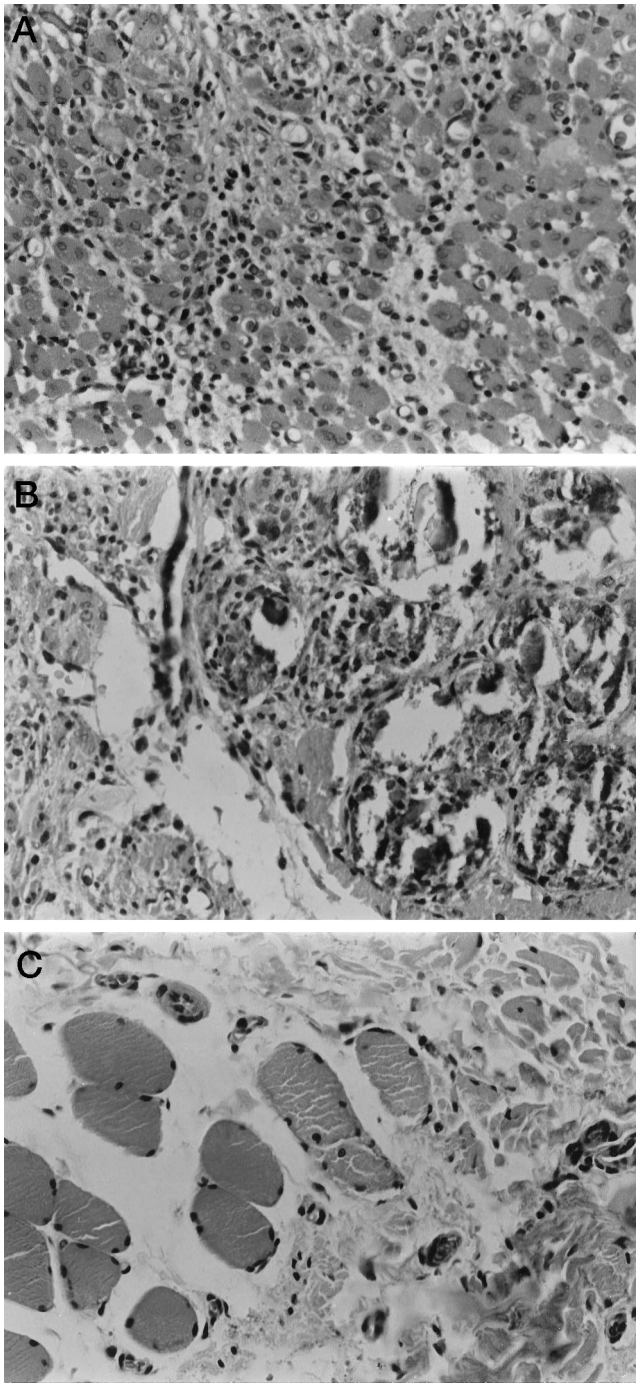

Figure 5. Light microscope photographs of hematoxylin and eosin-stained sections of injured muscle tissue from the control group (A), corticosteroid group (B), and anabolic steroid group (C) at day 7. (original magnification, ×20)

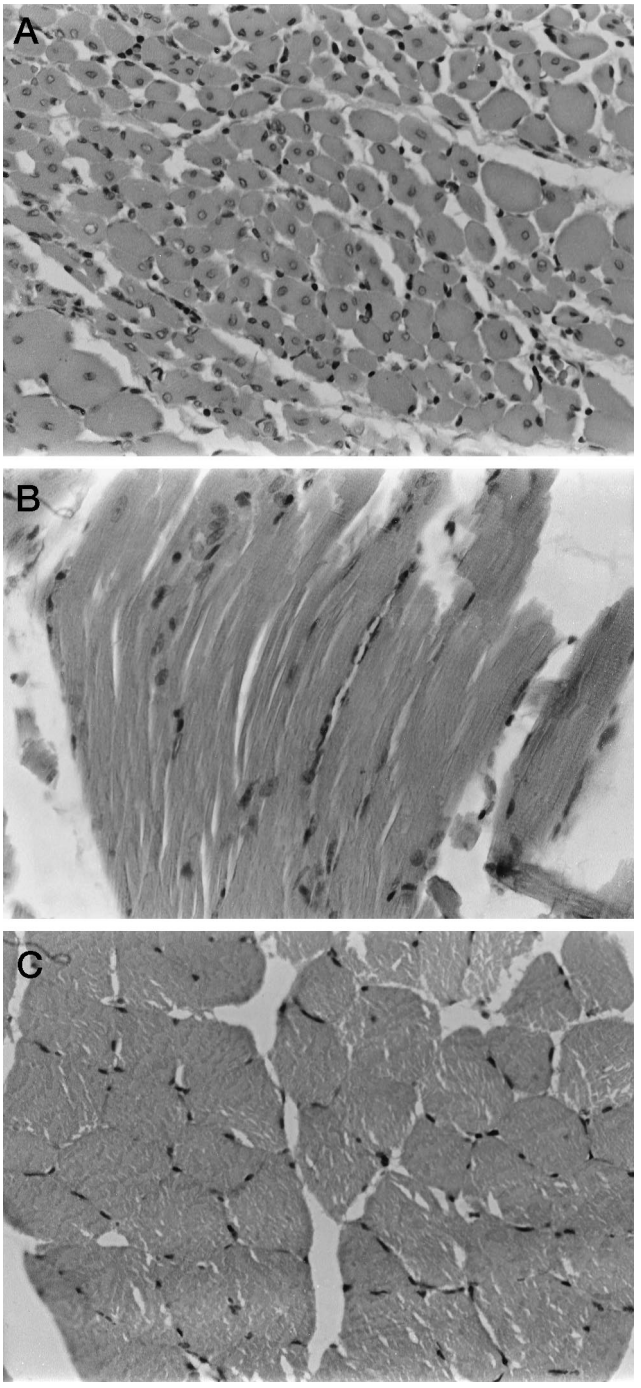

Figure 6. Light microscope photographs of hematoxylin and eosin-stained sections of injured muscle tissue from the control group (A), corticosteroid group (B), and anabolic steroid group (C) at day 14. (original magnification, ×20)

Histology

Qualitative analysis of injured muscles in the three groups was performed. No attempt to quantify these observations was made. At day 2, muscles from the anabolic group appeared similar to muscles from the control group. Hematoma was evident, as well as a brisk inflammatory reaction with marked interstitial edema. In the corticosteroid group, however, a marked decrease in tissue cellularity was observed, with fewer inflammatory cells and minimal edema (Fig. 4). At 7 days, control muscles showed evidence of removal of the necrotic tissue, dispersal of the

inflammatory cells, and infiltration. Anabolic muscles showed a similar progression of healing. Corticosteroid muscles, however, showed evidence of a delayed inflammatory response, with relatively more polymorphonucleocytes and macrophages, a paucity of fibroblasts and myotubes, and residual necrotic tissue (Fig. 5). At 14 days, control and anabolic muscles looked very similar to normal muscle, with clearing of necrotic tissue, regeneration of fibers, and relatively normal tissue architecture. Corticosteroid muscles showed marked atrophy, disorganized muscle fibers, and disruption of normal tissue architecture (Fig. 6).

DISCUSSION

Effect of Anabolic Steroid

Animals in the anabolic steroid group experienced a minimal increase in body weight relative to the control animals. Other experimental studies have reported mixed results of body weight measurements, with most reporting no gain in weight.[29,34–36] The different results are most likely due to multiple compounding variables, such as diet, exercise regimen, and method of measuring body weight. Our animals were given food ad libitum and were not exercised beyond normal cage movements. Weight was measured on a simple balance scale, with no attempt at differentiating lean body mass from total body weight. Our measurements indicate that any effect on body weight by anabolic steroids under such conditions is at best minimal.

Results from testing of force-generating capacity indicate that anabolic steroids may have a beneficial effect on healing muscle in the long term. The idea that these steroids accelerate the healing process is not new. A 1967 study found that a testosterone derivative (methandrostenolone) increased the number of inflammatory cells as well as muscle progenitor cells in the injured muscle relative to controls at 8 and 27 days.[33] In our model, in the short term there was relatively little effect of the drug on the healing muscle both with respect to the control group and to the contralateral uninjured muscle. In the long term, however, injured muscles were significantly stronger than control group muscles in twitch force at day 14, indicating a possible aid to the healing process. A similar trend was seen in tetanic contraction force in these muscles. It may be that a longer time period is necessary to observe the full effects of the anabolic steroid. Although this increase in strength relative to the saline-treated control group muscles may have been due to the increase in total body weight, the uninjured muscles in the anabolic group did not become stronger than their counterparts in the control group. We therefore find it unlikely that this increase in strength is due to size differences between animals. The preferential effect on twitch force may be due to a differential effect of anabolic steroids on the various muscle fiber types recruited in twitch versus tetanic contraction. Other studies have shown this fiber type-specific effect of anabolic steroids as well.[5,29–31]

Interestingly, in addition to becoming stronger than the control group injured muscles, the injured muscles treated with anabolic steroids also became stronger than their contralateral uninjured muscles in all cases. This may be explained if we consider the possible mode of action of anabolic steroids as outlined by Haupt and Rovere.[11] These steroids seem to counteract the catabolic state, whether it is caused by extreme exercise, malnutrition, or extensive muscle injury. Injured muscles have been shown to exhibit this catabolic state, and, while the stress to the animal may become systemic, presumably the injured muscle is in a more acute state of catabolism than the uninjured muscle and thus benefits more from the presence of the anabolic steroid.

Histologically, we observed an increase in the number of inflammatory cells, with pronounced interstitial edema in the short term. This may actually be detrimental to the healing muscle. In the long term, however, we saw changes most consistent with the rapid healing and restoration of force-generating capacity. The tissue was more highly organized and appeared much closer to normal than muscles treated with corticosteroids.

Effect of Corticosteroid

Animals in the corticosteroid group lost a significant amount of weight compared with the control animals. This confirms a large body of research that shows that these steroids are catabolic and promote overall negative nitrogen balance and loss of muscle. This effect makes it difficult to compare directly the long-term effects of the steroids on the healing muscle relative to saline-treated control muscles. However, the early, transient recovery of force-generating capacity in the muscles treated with corticosteroids is a surprising finding. Histologically, these muscles show a less robust inflammatory reaction. In 1967, Sloper and Pegrum[33] reported similar findings. They found a significant decrement in the number of inflammatory cells, including macrophages, polymorphonucleocytes, and histiocytes, in the injured muscles given cortisone. They also observed a relative paucity of microtubes and myoblasts in the area.

This inhibition of the inflammatory response may have a sparing effect on the local muscle tissue and perhaps on the animal as a whole in the short term.[20,33] We found increased strength in both the injured and uninjured muscles compared with the control and anabolic steroid groups, and an acceleration in the ability of the injured muscle to match its contralateral uninjured muscle in strength. In the long term, however, the effect on the muscle is not beneficial. The corticosteroids seem to cause an unwanted atrophy of both injured and uninjured muscles. In some animals, we found a nonhealed, angulated fracture of the tibia, accompanied by disordered muscle fibers and excessive atrophy. This was an incidental finding, but it may indicate that subtotal fractures in these animals did not heal because of the presence of the corticosteroid. These fractures, if present in the other groups, presumably healed without delay. More research using differing doses of the corticosteroid is needed to separate the effects of overall atrophy from effects on the healing

process of a contusion injury. Evidence at this point indicates that the long-term effects of these corticosteroids are detrimental.

This was a preliminary study, limited to a small number of animals. However, the results warrant further research into the effects of these drugs on muscle contusion healing. In addition to a larger number of animals, we are recommending a longer duration study and a better-controlled administration of drugs.

CONCLUSIONS

An anabolic steroid had a relatively minimal effect on the early recovery of force-generating capacity in our model of muscle contusion injury. Evidence indicates that these steroids may enhance the healing process in the long term, however, with increased force-generating capacity in injured muscles. In contrast, a corticosteroid, while speeding the recovery of strength in the short term, exerted a combined effect on muscle mass and tissue regeneration that seemed to be detrimental to the healing process in the long term.

REFERENCES

1. Bass AL, Robertson I: Injuries of the leg in football and ballet. *Proc R Soc Med 60:* 527–532, 1967
2. Canale ST, Cantler Ed Jr, Sisk TD, et al: A chronicle of injuries of an American intercollegiate football team. *Am J Sports Med 9:* 384–389, 1981
3. Crisco JJ, Jokl P, Heinen GT, et al: A muscle contusion injury model: Biomechanics, physiology, and histology. *Am J Sports Med 22:* 702–710, 1994
4. Damron C, Hoerner E, Shaw J: Monitoring sports injuries, in Vinger PF, Hoerner E (eds): *Sports Injuries. The Unthwarted Epidemic.* Littleton, MA, PSG Publishing Company, Inc, 1986
5. Exner GU, Staudte HW, Pette D: Isometric training of rats—Effects upon fast and slow muscle and modification by an anabolic hormone (nandrolone decanoate). I. Female rats. *Plugers Arch 345:* 1–14, 1973
6. Fisher BD, Baracos VE, Reid DC: Effect of systemic inhibition of prostaglandin synthesis on muscle protein balance after trauma in the rat. *Can J Physiol Pharmacol 69:* 831–836, 1991
7. Garret WE Jr: Muscle strain injuries: Clinical and basic aspects. *Med Sci Sports Exerc 22:* 436–443, 1990
8. Goldberg AL: Protein turnover in skeletal muscle. II. Effects of denervation and cortisone on protein catabolism in skeletal muscle. *J Biol Chem 244:* 3223–3229, 1969
9. Goldberg AL, Goodman HM: Relationship between cortisone and muscle work in determining muscle size. *J Physiol (Lond) 200:* 667–675, 1969
10. Griggs RC, Kingston RF, Jozefowicz RF, et al: Effect of testosterone on muscle mass and muscle protein synthesis. *J Appl Physiol 66:* 498–503, 1989
11. Haupt HA, Rovere GD: Anabolic steroids: A review of the literature. *Am J Sports Med 12:* 469–484, 1984
12. Hickson RC, Czerwinski SM, Falduto MT, et al: Glucocorticoid antagonism by exercise and androgenic-anabolic steroids. *Med Sci Sports Exerc 22:* 331–340, 1990
13. Hickson RC, Davis JR: Partial prevention of glucocorticoid-induced muscle atrophy by endurance training. *Am J Physiol 241:* E226–E232, 1981
14. Hickson RC, Heusner WW, Van Huss WD, et al: Effects of an anabolic steroid and sprint training on selected histochemical and morphological observations in rat skeletal muscle types. *Eur J Appl Physiol 35:* 251–259, 1976
15. Holbrook TL, et al: *The Frequency of Occurrence, Impact, and Cost of Musculoskeletal Conditions in the United States.* Park Ridge, IL, American Academy of Orthopaedic Surgeons, 1984
16. Jackson DW, Feagin JA: Quadriceps contusions in young athletes: Relation of severity of injury to treatment and prognosis. *J Bone Joint Surg 55A:* 95–105, 1973
17. Jarvinen M: Immobilization effect on the tensile properties of striated muscle: An experimental study in the rat. *Arch Phys Med Rehabil 58:* 123–127, 1977
18. Jarvinen M: Healing of a crush injury in rat striated muscle. 4. Effect of early mobilization and immobilization on the tensile properties of gastrocnemius muscle. *Acta Chir Scand 142:* 47–56, 1976
19. Jarvinen MJ, Lehto MUK: The effects of early mobilisation and immobilisation on the healing process following muscle injuries. *Sports Med 15:* 78–89, 1993
20. Jarvinen M, Lehto M, Sorvari T, et al: Effect of some anti-inflammatory agents on the healing of ruptured muscle. An experimental study in rats. *J Sports Traumatol Rel Res 14:* 19–28, 1992
21. Jarvinen M, Sorvari T: Healing of a crush injury in rat striated muscle. 1. Description and testing of a new method of inducing a standard injury to the calf muscles. *Acta Pathol Microbiol Scand [A] 83:* 259–265, 1975
22. Karpakka JA, Pesola MK, Takala TES: The effects of anabolic steroids on collagen synthesis in rat skeletal muscle and tendon: A preliminary report. *Am J Sports Med 20:* 262–266, 1992
23. Kayali AG, Young VR, Goodman MN: Sensitivity of myofibrillar proteins to glucocorticoid-induced muscle proteolysis. *Am J Physiol 252:* E621–E626, 1987
24. Mishra DK, Fridén J, Schmitz MC, et al: Anti-inflammatory medication after muscle injury: A treatment resulting in short-term improvement but subsequent loss of muscle function. *J Bone Joint Surg 77A:* 1510–1519, 1995
25. Odedra BR, Bates PC, Millward DJ: Time course of the effect of catabolic doses of corticosterone on protein turnover in rat skeletal muscle and liver. *Biochem J 214:* 617–627, 1983
26. Rannels SR, Jefferson LS: Effects of glucocorticoids on muscle protein turnover in perfused rat hemicorpus. *Am J Physiol 238:* E564–E572, 1980
27. Robinson AJ, Clamann HP: Effects of glucocorticoids on motor units in cat hindlimb muscles. *Muscle Nerve 11:* 703–713, 1988
28. Ryan JB, Whettler JH, Hopkinson WJ, et al: Quadriceps contusions. West Point update. *Am J Sports Med 19:* 299–304, 1991
29. Saborido A, Vila J, Molano F, et al: Effect of anabolic steroids on mitochondria and sarcotubular system of skeletal muscle. *J Appl Physiol 70:* 1038–1043, 1991
30. Salmons S: Myotrophic effects of anabolic steroids. *Vet Res Commun 7:* 19–26, 1983
31. Seene T, Viru A: The catabolic effect of glucocorticoids on different types of skeletal muscle fibres and its dependence upon muscle activity and interaction with anabolic steroids. *J Steroid Biochem 16:* 349–352, 1982
32. Shoji S, Pennington RJT: The effect of cortisone on protein breakdown and synthesis in rat skeletal muscle. *Mol Cell Endocrinol 6:* 159–169, 1977
33. Sloper JC, Pegrum GD: Regeneration of crushed mammalian skeletal muscle and effects of steroids. *J Pathol Bacteriol 93:* 47–63, 1967
34. Tingus SJ, Carlsen RC: Effect of continuous infusion of an anabolic steroid on murine skeletal muscle. *Med Sci Sports Exerc 25:* 485–494, 1993
35. Van Zyl CG, Noakes TD, Lambert MI: Anabolic-androgenic steroid increases running endurance in rats. *Med Sci Sports Exerc 27:* 1385–1389, 1995
36. Witzmann FA: Soleus muscle atrophy in rats induced by cast immobilization: Lack of effect by anabolic steroids. *Arch Phys Med Rehabil 69:* 81–85, 1988