Effect of steroid injections on the rotator cuff: An experimental study in rats

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The aim of this study was to evaluate the effects of repeated steroid injections into the subacromial space. Thirty rats were injected either 3 or 5 times with triamcinolone in a dosage equivalent to that given to human beings or 3 or 5 times with saline into the subacromial space. One rat received no injection. The supraspinatus and infraspinatus tendons were evaluated macroscopically and microscopically. Two different staining methods were used on each sample including hematoxylin eosin and Miller’s elastin/van Gieson’s solution. After 5 steroid injections, we found focal inflammation, necrosis, and fragmentation of collagen bundles in the tendon in 4 of 7 rats. The tendons of the controls showed a normal structure (P < .05). There were no pathologic changes among the rats that were injected with triamcinolone 3 times. These results show that repeated subacromial injections of triamcinolone may cause damage to the rotator cuff of the rat. This finding may indicate cautious use of subacromial steroid injections in human beings.

Repeated subacromial steroid injections are often used in patients with shoulder pain. Several clinical reports describe ruptures of such tendons as the Achilles and patellar tendons,13,19 and the medial collateral ligament of the knee.23,24 Several authors have studied preinjured tissue,6,9,20,24 and some have studied intact tendons or ligaments.1,17,22 Some authors found changes in the microscopic morphologic features of the tendons such as necrosis1 and nonparallel arrangement19 of collagen bundles after local steroid treatment, whereas others14,20 report no clear histologic or biomechanical changes. To our knowledge, this is the first study to describe the effect of local subacromial steroid injections on the rotator cuff.

The anatomy of the rotator cuff is unique. It has a bursa and a bone on one side and a joint cavity on the other side. The shoulder of the rat resembles the human shoulder and is an appropriate model for studies of the shoulder.22,26,28,29 The aim of this study was to evaluate whether triamcinolone given repeatedly into the subacromial space of the shoulder of the rat would be deleterious to the supraspinatus and infraspinatus tendons.

MATERIALS AND METHODS

Thirty-six Sprague-Dawley female rats were used. They were 3 months old and weighed 290 ± 18 grams. To ensure that the injections were placed correctly, subacromial injections with diluted methylene blue were performed in 3 rats. After dissection of these shoulders, the dye was found in the subacromial space each time. There were no intratendinous injections. These 3 rats were not included in the study.

The rats were randomly assigned to either subacromial injections of 5 µl (0.3 mg/kg of body weight) triamcinolone as a crystal suspension [Lederspan, Wyeth Lederle.
St Davis, Philadelphia), a dose equivalent to that given to human beings, or subacromial injections of 5 µL saline (9 mg/mL). All rats were injected in their left shoulder under a short anaesthetic induced by carbon dioxide. A sterile needle was used (Microlance 3, 27 G3/4, 0.4x19, Nr 20, Becton Dickinson, Drogheda, Ireland).

One group of 8 rats received a subacromial injection of triamcinolone in their left subacromial space once a week for 3 weeks. Another 8 rats were injected with triamcinolone once every other week for 8 weeks. One of the rats in the second group died because of an overdose of carbon dioxide at the first injection. The rats in the 2 control groups, each consisting of 7 rats, were injected with saline, 1 group 3 times a week for 3 weeks, the other 5 times every other week for 8 weeks. One rat in the latter group died at the fourth injection because of an overdose of carbon dioxide. Finally, 1 rat did not receive any injection. All injections were performed under sterile conditions. The rats behaved normally and there were no signs of infections.

The supraspinatus and infraspinatus tendons were removed 1 week after the last injection and immediately placed in a 4% phosphate-buffered formaldehyde solution. Before removal, the tendons were investigated macroscopically. The tendons were then embedded in paraffin, sectioned longitudinally into 5 µm sections and stained with hematoxylin eosin and Miller’s elastin/van Gieson’s solution. A blinded histologic evaluation was performed by the pathologist (L.F.).

The paired t test (2-tailed) and Fisher’s exact test (1-tailed) were used for statistical analysis. The study was approved by the local ethics committee.

RESULTS

Macroscopic morphology

There were no macroscopic changes in the normal structure of the tendon, either among the 7 rats that received saline or among the 8 rats that were injected with triamcinolone 3 times.

In 2 of the 7 rats that were injected with triamcinolone 5 times, the normal structure of the tendon was clearly changed. The tendon had become more white and less smooth (Table I). The 6 saline controls showed no changes in the normal structure of the tendon.

Microscopic evaluation

There were no findings indicating necrosis of collagen bundles and no inflammatory cells such as macrophages or giant cells in the tendons of the rats that were injected 3 times with triamcinolone. There was 4 of 7 rats that were injected with triamcinolone 5 times, microscopic changes in the structure of
the tendon could be seen. Inflammatory cells, predominantly macrophages and giant cells, were found in great numbers in the tendons between the collagen bundles (Figure 1). In addition, there were clear signs of necrosis and fragmentation of the collagen bundles (Figures 2 and 3). Among the 6 rats injected with saline, there were no signs of necrosis or inflammation. The incidence of histopathologic change differed significantly between the rats treated with triamcinolone (4 of 7) and the rats treated with saline (0 of 6) (P < .05).

Body weight

Of the rats treated with triamcinolone, the weight of those injected every week dropped by 14 ± 8 g/week, whereas the weight of those injected every other week dropped by 1 ± 4 g/week. The weight of rats that were injected with saline 3 times a week increased by 12 ± 4 g/week. Those that were injected with saline 5 times gained 7 ± 2 g/week (Table II). The difference in weight between saline-treated rats and triamcinolone-treated rats was significant (P < .001). The weight of the untreated control rat increased by 5 g/week.

DISCUSSION

Since the 1950s the adverse effects of corticosteroids on tendons and ligaments have been a matter of debate. Many anecdotal clinical reports describe tendon ruptures after local deposition of steroid but the scientific value of these reports is regarded as limited. Many animal experiments have been performed, but no report describes the effects of corticosteroid injections on the tendons of the rotator cuff. The effects of steroids may vary between different anatomic structures such as tendons and ligaments and between different anatomic sites. In this study we focused on the tendons of the rotator cuff because of their unique anatomic relations to a bursa and a bone on one side and a joint on the other side. We chose the rat shoulder as a model because of its anatomic resemblance to the human shoulder. The tendons of the rotator cuff of the rat are well defined, as is the subacromial bursa.

After 3 subacromial injections of triamcinolone, the morphologic features of the tendons were still normal. However, changes were obvious after 5 steroid injections. In 2 of 7 cases, the tendons appeared atrophic at the macroscopic evaluation. The microscopic evaluation revealed inflammatory cell reaction, necrosis, and fragmentation of the collagen bundles in 4 of 7 tendons. In contrast to these findings, there were no changes in the normal structure of the tendons among the rats in the control groups. These results are consistent with those of Balasubramaniam and Prathap and Kennedy and Baxter Willis, who found inflammatory cells, collagen necrosis, and disruption of collagen fibers 1 week after injection of hydrocortisone acetate or betamethasone. In both these studies, however, the steroid was injected into the Achilles tendon. Unversfeld and Oliu and Krulik and Luhnow reported similar findings after intratendinous steroid injections. Mackie et al injected methylprednisolone into normal patellar tendons in rabbits 3 to 4 times but did not find any adverse effects on the biomechanical properties of the tendons. They did not perform a histologic evaluation. Noyes et al found decreased biomechanical strength of the anterior cruciate ligament after intraarticular injections of methylprednisolone acetate. They did not find any signs of collagen necrosis or inflammatory cell reaction, although the biomechanical testing showed impaired tendon and ligament strength, respectively. Biomechanical testing may reveal damage to tendinous tissue before histologic changes appear.

Some kind of systemic effect of the local steroid injections can be assumed because the rats in this study that received triamcinolone injections decreased in average body weight. This observation is consistent with the findings of Koehler et al but in contrast to those of Kapetanos, who did not find differences in body weight after repeated triamcinolone injections in the rabbit.

The results of this study show changes in the normal structure of the supraspinatus and infraspinatus tendons after repeated subacromial injections of triamcinolone in the rat. Although the response to corticosteroids may differ between species, our findings support the cautious use of subacromial corticosteroid injections in human beings.

REFERENCES


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<th>Table II Change in body weight per week</th>
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<td>Triamcinolone x3</td>
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P < .001. Significance was calculated with a 2-tailed paired t test.