The Effects of Short- and Long-Term Corticosteroid Treatment on Rat Diaphragm Contractility and Fatigue*

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Male Wistar rats received dexamethasone (1.5 mg/kg/day) hind-limb injections for 2.5 weeks (D−2.5 wk, N = 10) and 10 weeks (D−10 wk, N = 9). Controls were pair-fed and injected daily with saline solution. All groups had similar weights initially (186 ± 2 g). Pneumonia was not a complication. Hemidiaphragm costal strips were bathed in modified Krebs (37°C) containing insulin and d-tubocurarine. At optimal length, isometric twitch (2 ms, sq wave) and tetanic tensions (400 ms trains at 10, 20, 60, and 100 Hz), normalized for muscle strip csa (g/cm²), were measured at baseline B1, after 10 min of fatiguing stimulation (5 impulses at 5 Hz; 30 trains/min) and after 10 min of recovery. The fatigue resistance index (FRI) was defined as fatigue index/baseline index.

Compared to pair-fed controls, D−2.5 and D−10 week administration produced decreases in body and diaphragm weights (Table 1). In maturing rats, diaphragm strength increased with short-term treatment and did not change with long-term treatment. Significantly increased fatigue resistance was noted over both time spans. These findings might be explained by type II atrophy shown in rat hind-limb steroid studies (Robinson, Muscle Nerve 1988;703).

Histopathologic Effect of Corticosteroids on Respiratory Muscles in the Rabbit

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Corticosteroids are known to preferentially induce myopathy in peripheral muscles composed primarily of type IIB fibers, while minimally affecting those with mostly type I fibers. Since the diaphragm is composed of predominantly type I fibers and we have previously demonstrated that corticosteroids reduce respiratory muscle endurance but not strength, we wondered whether corticosteroids induce pathologic changes in respiratory muscles other than those found in peripheral skeletal muscles and whether specific muscle fiber types were affected.

We therefore examined muscle pathology and fiber type in rabbits randomized to receive either cortisone or placebo for 3 weeks. Corticosteroids induced expected pathologic changes in the extensor digitorum longus (weight—corticosteroid: 2.12 vs placebo: 3.86 g, cross-sectional area—corticosteroid: 0.59 vs placebo: 1.22 cm²) and in the soleus (1.05 vs 2.05 g, 0.60 vs 0.62 cm²). There was a marked decrease in the diaphragm (4.26 vs 6.22 g, 2.68 vs 3.46 cm²) and a lesser decrease in the sternoleidomastoid (1.46 vs 1.83 g, 0.28 vs 0.38 cm²). The percentage of cross-sectional area containing muscle fibers was significantly reduced in the extensor digitorum longus in the corticosteroid-treated animals (78 ± 2 vs 89 ± 2%, p < 0.05), with no change in the soleus (93 ± 1 vs 93 ± 1%). There was also a significant reduction in the diaphragm (65 ± 3 vs 88 ± 2%, p < 0.01) and the intercostal 75 ± 3 vs 90 ± 2%, p < 0.01, while there was no change in the sternoleidomastoid (81 ± 3 vs 88 ± 1%, NS). There was no significant change in muscle fiber composition in any of the muscles following corticosteroids.

On the other hand, there was a significant decrease in mean cross-sectional area of type I muscle fibers (15.1 ± 1.2 vs 22.2 ± 1.1 × 10⁻⁴ mm², p < 0.01) and type IIA muscle fibers (23.6 ± 2.5 vs 30.9 ± 2.2, p < 0.05) in the diaphragm and a significant decrease in mean cross-sectional area of type IIB muscle fibers in the diaphragm (26.6 ± 3.1 vs 38.7 ± 4.3, p < 0.05), intercostal (23.4 ± 3.0 vs 37.3 ± 3.1, p < 0.01), sternoleidomastoid (26.9 ± 1.2 vs 39.2 ± 1.4, p < 0.01) and extensor digitorum longus (21.4 ± 1.7 vs 44.3 ± 2.6, p < 0.01).

We conclude that (1) corticosteroids induce greater atrophy and pathologic changes in the diaphragm than in other respiratory or peripheral muscles; (2) the severity of atrophy and pathologic change observed in the diaphragm following corticosteroids appears to be related to a selective effect of corticosteroids on oxidative fibers (types I and IIA) in the diaphragm; and (3) the effect of corticosteroids on other respiratory muscles is more typical of peripheral muscles, i.e., selective type IIB muscle fiber atrophy. We speculate that the alterations in respiratory muscle endurance following corticosteroid administration may be caused by the predilection of corticosteroids to induce atrophy in diaphragm oxidative muscle fibers.

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