Effects of Vitamin D on rat skeletal muscle regeneration following open muscle injury

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ABSTRACT INTRODUCTION:

Muscle injuries present a challenging problem in current orthopedic and trauma surgery. Until now, a broad spectrum of cytokines, growth factors and vitamins is known to facilitate muscle regeneration during muscle injury and neuromuscular diseases. Vitamin D is a secosteroid that is produced in the skin and is synthesized in the liver and kidney in its biologically active form, 1,25-Dihydroxyvitamin D. So far there is increasing evidence that Vitamin D positively affects the muscle function as well as the muscle force [1]. In the current study we tested for the first time the hypothesis that application of Vitamin D could accelerate muscular regeneration after skeletal muscle injury in rats.

METHODS:

For this purpose we anesthetized 53 male Wistar rats (275-300 g body weight) with pentobarbital sodium (60 mg/kg body weight i.p.) and induced a blunt injury of the left soleus muscle by using an instrumented clamp as described before [2]. All animals received immediately after trauma a single dose of either 8.3 mg/kg body weight Vitamin D i.p. (Vit-D) or equivalent volumes of medium-chain triglycerides as vehicle solution i.p. (control). Subsequent observations were performed at day 1, 4, 14 (n=7 animals per time point and group) and day 42 (n=7 animals for the Vit-D group and n=4 animals for the control group) after injury induction. After bilateral stimulation of the sciatic nerve fast twitch (stimulation with 9 mA/75 Hz, 5 times for 0.1 s in 5 s intervals) and tetanic forces (stimulation with 9 mA/75 Hz, 5 times for 3 s in 5 s intervals) of the soleus muscles were analyzed and given in percent of the forces of the non-injured muscle. By using immunohistochemistry and histology we analyzed the muscle cell proliferation (BrdU immunohistochemistry) and the muscle cell apoptosis (TUNEL histology). Data are given as means ± standard error of the mean (SEM). Differences between groups were assessed using a t-test. Statistical significance was set at p<0.05.

RESULTS SECTION:

Muscle strength analysis revealed recovery of contraction forces to 91±1, 13±2, 48±5 and 75±8 % (tetanic force) and to 12±2, 20±2, 56±7 and 75±9 % (twitch force) at 1, 4, 14 and 42 days of observation in vehicle-treated animals. Vitamin D could slightly increase the contractile forces to 11±2, 19±2 and 53±4 % (tetanic force) and to 18±4, 25±3 and 61±9 % (twitch force) within the first 14 days. At day 42 a significant increase of the tetanic force to 94±4 % was observed as well as a slight increase of the twitch force to 77±10 % compared to the control group. This enhancement of muscle contraction was preceded by a significant increase of cell proliferation (BrdU-positive cells/mm²: 163±19 vs. vehicle: 76±27) and a significant decrease of cell apoptosis (TUNEL-positive cells/mm²: 18±2 vs. vehicle: 29±2) at day 4 after injury (Fig. 2a and b).

At later time points, no major difference between the number of proliferating and apoptotic cells was noted, and injured muscles of Vitamin D treated animals reached mean values of the control group.

DISCUSSION:

The present study demonstrates that Vitamin D enhances the biomechanical characteristics of the injured muscle by significantly improving the tetanic force 42 days after injury. Furthermore we could show that the functional restoration of the muscle is based on an increased cellular turnover, i.e. increased proliferation and decreased apoptosis at day 4 after injury. Overall this data support our primary hypothesis that Vitamin D induces regenerative processes in injured muscle. Thus, Vitamin D may represent a promising therapeutic option to optimize recovery after injury.

REFERENCES: