IMMOBILIZATION AND STRETCH EFFECT ON THE CONCENTRATION OF
TYPE IV COLLAGEN AND COMPOUNDS RELATED TO ITS SYNTHESIS
AND DEGRADATION IN MUSCLES

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INTRODUCTION

Immobilization has been shown to cause muscle atrophy (e.g. Goldspink, 1977),
down regulation of total (e.g. Karpakka et al. 1991) and fibrillar collagens (type I and
II) (Han, X; Wei, W; Myllyla, R; Virtanen, P; Karpakka, J; Takala, T.E.S.,
unpublished). The atrophy and decrease in collagen synthesis rate are counteracted
by stretch (e.g. Savolainen et al. 1988). Type IV collagen is the main component of
basement membranes surrounding muscle fibers. Type IV collagen is degraded by
MMP-2 which is inhibited by TIMP-2 (Stetler-Stevenson et al. 1989). The purpose
of this study was to find out the early effects of immobilization in shortened and
lengthened positions on concentration of type IV collagen and compounds related to
the synthesis and degradation of type IV collagen in rat skeletal muscle.

MATERIAL AND METHODS

Age-matched adult male Sprague-Dawley rats were randomized into six different
experimental groups and a control group, 8-9 animals in each group. The right
hindlimb of the experimental animals was immobilized with a plaster of Paris, so that
the ankle joint was in full plantar flexion (150-160° ankle between foot and leg) or in
dorsiflexion (30-40° ankle). The length of the immobilization period was 1, 3 and 7
days. The muscles used in this study were gastrocnemius (GM) and tibialis anterior
(TA). mRNA levels were analyzed using Northern and slot blot hybridization and
densitometry. Concentration of type IV collagen was analyzed using
radioimmunoassay for detecting 7-S collagen, which locates at the aminoterminal
end of type IV collagen (Timpl et al. 1979). Zymography was used for analyzes of
gelatinolytic activity of proMMP-2. Statistical evaluation was performed using
nonparametric Mann-Whitney U-test.

RESULTS

Weights of GM and TA were decreased significantly after 3 and 7 days of
immobilization. The decrement was more pronounced in GM immobilized in
shortened position than in lengthened position. The difference was statistically significant (p<
0.05) after 7 days of immobilization. mRNA level of type IV collagen was decreased
after 1, 3 and 7 days of immobilization in GM, whereas no changes were observed in
these levels in TA. Concentration of type IV collagen decreased after 1 and 3 days of
immobilization in GM, but no changes were found in TA. MMP-2 mRNA level
increased in both GM and TA after 3 and 7 days of immobilization, the increase
being more pronounced in shortened than in lengthened muscle (p< 0.05 after 7 days
immobilization in TA). Gelatinolytic activity of proMMP-2 was increased after 3
days in shortened GM and after 1 and 7 days in lengthened TA. In GM, the increase
was prevented with stretch. No changes in mRNA level of TIMP-2 were seen in GM
within 7 days of immobilization, but in TA there was an increase after 3 and 7 days in shortened position.

DISCUSSION

In GM, there is evidence of reciprocal regulation in the synthesis of type IV collagen and its degradation towards negative type IV collagen balance by muscle immobilization. This negative balance could be a part of decrease in basement membrane area due to muscle fiber atrophy. The muscle atrophy and degradation of type IV collagen is partly prevented by stretch. mRNA data suggests that the synthesis of type IV collagen in TA was not affected by immobilization within 7 days. There was even a slight increase in type IV collagen concentration in shortened muscle. Increased TIMP-2 mRNA level together with unchanged gelatinolytic activity of proMMP-2 suggest that increased inhibition of degradation may participate to this elevation. Immobilization has been shown to cause transformation of fast glycolytic fibers (lib) towards more oxidative forms (Laurila et al. 1991). Muscles which have predominantly type I fibers contain more type IV collagen than muscles with predominantly type lib fibers (Kovanen et al. 1988). Thus, muscle fiber transition towards oxidative types may be associated with the unchanged or even elevated type IV collagen content in TA inspite of muscle atrophy.

REFERENCES


