Enhanced lipid peroxidation in Duchenne dystrophy muscle may be secondary to muscle damage

Abigail Foxley, Richard H.T. Edwards and Malcolm J. Jackson

Muscle Research Centre, Department of Medicine, University of Liverpool, P.O. Box 147, Liverpool L69 3BX.

Although it is now recognised that Duchenne muscular dystrophy (DMD) results from a lack of dystrophin in muscle the mechanism by which this deficiency of this protein leads to the characteristic muscle damage and degeneration is currently unknown. Enhanced free radical-mediated lipid peroxidation has previously been suggested as a possible mechanism leading to degradation of muscle tissue in DMD [1-3] and increased amounts of malonaldehyde (or correctly thioarbituric acid-reactive substances) have been reported in muscle biopsy samples from patients with DMD [1-3], but not from patients with other forms of muscular dystrophy [4]. These findings suggested that the elevated lipid peroxidation products in DMD muscle were either a specific consequence of the biochemical defect in Duchenne or due to the greater amount of damage and degeneration generally seen in this disorder in comparison to other forms of muscular dystrophy. Increased lipid peroxidation has been suggested to occur as a consequence of non-specific damage to tissues rather than as a cause of it [5].

The mdx mouse has a genetic defect within the same region of the X-chromosome as patients with DMD and also lacks dystrophin in muscle [6]. However, the mdx mouse shows no obvious defect in muscle function and has much less apparent muscle damage and fibro-fatty replacement of muscle than patients with DMD [7]. We have therefore examined various indicators of lipid peroxidation in muscles from mdx and control mice in order to determine whether the enhanced lipid peroxidation products seen in DMD are likely to be a specific consequence of dystrophin deficiency.

Control C57 Bl/10 and mutant C57 Bl/10 mdx mice of both sexes and of six weeks or six months of age were killed by cervical dislocation and the gastrocnemius muscles rapidly removed and analysed for their basal content of thiobarbituric acid-reactive substances (TBARS) as previously described [8]. Muscle homogenates were also incubated at 37°C for 2 hours in the presence of ascorbate and FeSO₄ prior to analysis of TBARS [8]. Muscles were also analysed for diene conjugates and lipid soluble, fluorescent Schiff's bases [2].

Results of TBARS analyses are shown in figure 1. No difference between the TBARS content of mdx and control muscles was seen at either age studied. There was a small, but significant (P 0.05) elevation of the TBARS produced following 2 hours incubation in the 6 week old animals compared to control, but this was not seen in the 6 month old animals. No difference between the diene conjugates and lipid soluble Schiff's bases in mdx and control muscle was seen at either age studied.

These results therefore do not support the hypothesis that a lack of dystrophin causes degeneration of muscle via an increase in non-enzymatic lipid peroxidation. The increase in TBARS in mdx homogenates produced on incubation of the samples from 6 week old mice may reflect a decreased antioxidant potential of these samples, but the significance of this is not clear since it was not previously seen in DMD [2]. The results therefore suggest that the increased lipid peroxidation products seen in DMD muscle are more likely to be a secondary consequence of the large amount of muscle damage which occurs in this disease.

The authors would like to acknowledge financial support from the Muscular Dystrophy Group of Great Britain and Northern Ireland, Dr. P. Maclellan for helpful discussions and Dr. T. Partridge for supplying breeding pairs of C57 Bl/10 mdx mice.

Abigail Foxley, Richard H.T. Edwards and Malcolm J. Jackson

Muscle Research Centre, Department of Medicine, University of Liverpool, P.O. Box 147, Liverpool L69 3BX.