



THE EFFECT OF THEOPHYLLINE ON THE RESPIRATORY

AND QUADRICEPS FEMORIS MUSCLES IN MAN.

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ABSTRACT

Twitch tension in fresh and fatigued skeletal muscle strips is increased by methylxanthines. In animals, a significant inotropic effect occurs only at theophylline concentrations which are above the therapeutic range in man, while changes at therapeutic concentrations of theophylline in normal subjects and in patients are inconsistent. It has been suggested that patients with respiratory muscle weakness or who are at risk of fatigue may benefit from enhanced respiratory muscle contractility with dimethylxanthines. The magnitude of the effect on respiratory muscle contractility at therapeutic concentrations, and the effect on maximal contractions are not known.

The action of dimethylxanthines on the contractility of respiratory and quadriceps femoris muscle in normal subjects and in patients at risk of respiratory muscle fatigue was assessed using accepted techniques.

The acute effects of aminophylline were investigated in two open studies. In four normal volunteers, twitch tension was not enhanced. However, in a quadriplegic patient, paced transdiaphragmatic pressure significantly increased by 12.6%.

The effect of chronic theophylline was studied in three double-blind randomised, placebo-controlled trials. In the first study of six normal subjects, theophylline had no effect on quadriceps strength, on fatigue-development, or on the shape of the fresh or fatigued frequency-force curve. However, a small treatment difference (1-2%) was noted in low frequency

(20Hz) contractions before and after fatigue.

In five normals, sniff transdiaphragmatic pressure significantly increased by 4.1%, but there were no changes in global respiratory or quadriceps muscle strength.

In 10 patients with chronic obstructive pulmonary disease there were increases in maximal inspiratory mouth pressures at residual volume and functional residual capacity of 11.4% and 18% respectively. Pulmonary function, six minute walk, breathlessness scores, maximal expiratory mouth pressures, and quadriceps strength did not differ between treatment periods.

In all studies, theophylline levels were within the therapeutic range.

Despite the small numbers, a positive inotropic action of theophylline was identified. The improvement in muscle contractility varied between studies: approximately 5% in normal subjects, and 15% in patients. The variable response may be related to the presence or absence of skeletal muscle weakness, fatigue, and factors which potentiate the development of fatigue, such as hypoxia, hyperinflation and raised inspiratory muscle work loads.