LETTERS

Serum LDH and exercise capacity in COPD

Lactate dehydrogenase (LDH) is the enzyme that catalyses the final step in the glycolytic metabolism, regenerating NAD^+ from reduced NADH, by conversion of pyruvate to lactate.[1] Recently, increased muscle LDH activity has been found in elderly male patients with chronic obstructive pulmonary disease (COPD) who were susceptible to contractile fatigue of the quadriceps femoris muscle following constant work rate cycle exercise performed at 80% of the predetermined peak work rate.[2] Moreover, increased resting serum LDH activity has been found in patients with COPD compared with healthy smoking and non-smoking peers.[3] To date, it remains unknown whether and to what extent increased resting serum LDH activity may be linked to a reduced functional exercise capacity and to self-reported daily symptoms of dyspnoea in patients with COPD.

Therefore, pulmonary function, functional exercise capacity (6 min walking distance, 2×), overnight fasting fat free mass (bioelectrical impedance assessment), the original Medical Research Council (MRC) dyspnoea grade and serum LDH activity were assessed in 178 elderly male patients with COPD who were referred for pulmonary rehabilitation to the Centre for Integrated Rehabilitation for Organ failure (CIRO) in Horn, The Netherlands (additional details on the methodology used can be found in the online repository facility).

On average, patients had moderate to severe COPD, impaired carbon monoxide transfer factor, normal body mass index and normal fat free mass index (table 1). In addition, most patients reported that they had to stop because of breathlessness after walking 100 m or after a few minutes of walking on the level.

Thirty patients (16.9%) had increased serum LDH activity (defined as >480 U/l). No significant differences were found in age, pulmonary function or body composition after stratification of the patients by normal or increased serum LDH activity. In contrast, patients with normal serum LDH activity had a significantly lower MRC dyspnoea grade and a higher functional exercise capacity than patients with increased serum LDH activity. This was also true after correction for height, age and body weight (table 1).

Approximately one-sixth of male patients with COPD who were referred for pulmonary rehabilitation had increased serum LDH activity. Although only a weak inverse relationship was found between functional exercise capacity and serum LDH activity ($r = -0.29$, $p = 0.0001$), we believe that the present findings can still be of clinical interest. Firstly, the statistically significant differences in the 6 min walking distance between patients with normal and increased serum LDH activity clearly exceeded the minimal clinically important difference of 54 m. Secondly, patients with increased serum LDH activity experienced a significantly higher sensation of dyspnoea during daily life, while no significant differences were found in age, lung function impairment or body composition. This may imply that increased serum LDH activity may be a reflection of qualitative and/or quantitative changes in the skeletal muscles of patients with COPD. Indeed, increased serum LDH activity may, at least in part, be a direct consequence of changes in the mitochondrial respiratory function and/or skeletal muscle fibre-type shifts in COPD.[4 5]

In conclusion, the present findings are hypothesis generating rather than definitive. In fact, future studies should take into account the fact that LDH is expressed as five isoenzymes, which were not assessed in the present study. Nevertheless, physical inactivity has been shown to shift fibre LDH isoenzymes from an oxidative to an anaerobic profile.[6]

Table 1 Patient results

	Total group	Normal LDH	Increased LDH	p Value
No of male patients	178	148	30	–
Age (y)	66.0 (9.2)	65.7 (9.0)	67.7 (10.4)	0.2832
FEV_1 (% predicted)	39.9 (14.2)	39.7 (13.6)	40.7 (17.5)	0.7350
TIco (% predicted)	48.2 (18.3)	48.0 (18.6)	49.8 (17.2)	0.6719
MRC dyspnoea grade	3.8 (1.1)	3.7 (1.2)	4.4 (0.9)	0.0050
BMI (kg/m^2)	25.1 (4.6)	24.8 (4.6)	26.4 (4.8)	0.0867
FFMI (kg/m^2)	17.3 (2.2)	17.2 (2.1)	17.8 (2.3)	0.1589
6MWD (m)	404.3 (130.1)	417.8 (128.4)	333.8 (117.2)	0.0016
6MWD (% predicted)	60.3 (18.9)	61.9 (18.6)	52.1 (19.0)	0.0114
Borg score D (points)	4.5 (2.2)	4.4 (2.2)	5.1 (2.1)	0.1124
Borg score F (points)	3.8 (2.3)	3.9 (2.3)	3.6 (2.4)	0.6004
LDH (U/l)	404.1 (96.0)	372.8 (57.5)	559.4 (98.8)	0.0001

Values are mean (SD).
6MWD, 6 min walking distance; BMI, body mass index; D, dyspnoea; F, fatigue; FEV_1, forced expiratory volume in 1 s; FFMI, fat free mass index; LDH, lactate dehydrogenase; MRC, Medical Research Council; TIco, carbon monoxide transfer factor; U/l, micromoles per minute/litre.

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► Additional details on methodology are published online only at http://thorax.bmj.com/content/vol63/issue5

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Adalimumab-induced bronchospasm: not a class effect

A 48-year-old man with rheumatoid arthritis (RA) was admitted with shortness of breath due to bronchospasm and hypoxaemia (PaO_2 5.9 kPa (44 mm Hg)). He had no history of pulmonary disease or allergy/atopy. About 3 years before this admission he was treated with infliximab. He was switched from infliximab to etanercept because of its more convenient subcutaneous form of administration. He was switched from etanercept to adalimumab because his RA persistently flared on the former treatment. Three days before admission he had received adalimumab for the second time. Blood count showed a new eosinophilia of 0.8×10^9/l (normal range 0–0.4). He was treated with inhalation medication (salbutamol and ipratropium bromide) and prednisolone 50 mg/day. Pulmonary function tests were performed 3 days after admission and showed an obstructive pattern: forced expiratory