Serum myosin light chain determinations in patients with inflammatory myopathy—a preliminary report

The determination of serum myosin light chain (MLC) has been used to detect myocardial infarction and to assess the extent of myocardial damage in a variety of myocardial disorders.\(^4\) This technique has improved diagnostic sensitivity and has provided a better correlation with left ventricular function compared with the routine serum creatine kinase (CK) determination. The technique has not previously been evaluated for the assessment of disease activity in the inflammatory myopathies.

Twenty seven measurements of both serum CK and MLC were made in 19 patients with established myositis. In five patients, two or more measurements at different times were available. All patients fulfilled at least three of the diagnostic criteria set by Bohan and Peter,\(^2\) and 17 had an inflammatory myopathy confirmed by biopsy. The table lists the patients' clinical characteristics. Patients were considered to have active disease if they exhibited progressive muscle weakness for the three months preceding the test, an increased CK concentration, or both; they were considered to have inactive disease if they exhibited no progressive muscle power for the three months preceding the test associated with a normal CK level. Muscle power was assessed by the modified sphygmonanometer technique; none of the patients had joint pain which could influence the assessment. The CK determination was performed by the routine biochemistry laboratory; normal values were <130 U/I for women and <160 U/I for men.

Serum MLC concentrations were determined by a liquid phase competitive radioimmunooassay using a mouse monoclonal antibody against MLC and an iodine-125 radiolabeled synthetic polypeptide as described by Nicol et al.\(^7\) Normal values were determined in 70 healthy individuals: the upper limit of normal (mean + 3 SD) was found to be 1 ng/ml. Variance in the assay was 17.3%. Statistical significance was calculated by Fischer exact test and Mann-Whitney U test.

Serum MLC concentrations in patients with active disease (median 31 ng/ml) were significantly greater than those in the patients with inactive disease (median 0.32 ng/ml) (p = 0.0002) (figure). In particular, all 17 measurements in patients exhibiting active disease were increased. Among these patients, serum MLC values were increased in three patients who were considered to have active disease (as defined above), despite normal CK concentrations; two of these three were not treated with corticosteroids and one was treated with prednisone 10 mg/day. In two patients, muscle biopsy confirmed an active inflammatory process. In nine patients with inactive disease, three of 10 measurements were elevated (>1 ng/ml). Further studies are needed to clarify the significance of these findings.

The relationship between serum MLC concentration and disease activity over time was examined in five patients. A marked reduction in serum MLC was noted when the disease became inactive (as defined above). In patients with active disease the median serum MLC concentration was 68.8 ng/ml, compared with 3.7 ng/ml in patients with inactive disease. In four patients, however, MLC values remained elevated for three months after normalisation of the CK concentration—at a time when the patients were considered clinically to have inactive disease. Further studies involving serial muscle biopsies from patients in this group will clarify the significance of this finding.

Our preliminary data in patients with inflammatory myopathies demonstrate increased serum MLC concentrations which correlate strongly with disease activity. Our results suggest that measurement of MLC concentrations may be advantageous in diagnosis and the evaluation of response to treatment. In myositis the response to treatment is particularly difficult to monitor because of the rapid normalisation of the electromyogram and CK levels. Whether

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**Clinical features of patients with myositis**

<table>
<thead>
<tr>
<th>Demographic details (n = 19)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>15</td>
</tr>
<tr>
<td>Oriental</td>
<td>3</td>
</tr>
<tr>
<td>Native Indian</td>
<td>20</td>
</tr>
<tr>
<td>Age (y)</td>
<td>53-3 (28-83)</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>136</td>
</tr>
</tbody>
</table>

**Diagnoses**

- Polymyositis: 6
- Dermatomyositis: 6
- Polymyositis/overlap: 4
- Systemic lupus erythematosus: 2
- Progressive systemic sclerosis: 1
- Mixed connective tissue disease: 1
- No with inclusion body myositis: 3
- Disease duration (y): 5-4 (0-1-18)

Absolute values or mean (range)
MLC concentrations will be useful in the assessment of such a response remains to be determined. A previous preliminary report revealed high MLC levels in 75% of patients with myositis, but a correlation with disease activity was not performed. Further prospective longitudinal studies are in progress to determine the utility of measuring MLC concentrations in myositis.

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**Decreased triglyceride levels with low calorie diet and increased renal excretion of uric acid in hyperuricaemic-hyperlipidaemic patients**

While the association between hyperuricaemia and hyperlipidaemia is well known, it has so far been poorly explained.1 The presence of external factors such as obesity, increased alcohol intake,2 or some nutritional habits3 in an individual was initially believed to cause both metabolic disturbances. However, this has been shown not to be the case in many instances; hyperuricaemia and hypertriglyceridaemia have been observed in the absence of those factors,4 and even ascribed to a common genetic basis.5 In addition, hyperuricaemic-hyperlipidaemic patients have been shown to exhibit decreased renal excretion of urate relative to hyperuricaemic-normolipidaemic individuals.6

In order to investigate alterations in the renal excretion of uric acid in relation to plasma concentrations of triglycerides, we carried out a dietary intervention study in two patient groups before and after low calorie dieting aimed to decrease their triglyceride concentrations.

We studied 15 primary hyperuricaemic patients (all men) and 15 primary hyperlipidaemic patients (all women). Subjects with plasma uric acid concentrations greater than 7 mg/dl were classed as hyperuricaemia, and those with values greater than 200 mg/dl as hyperlipidaemia. All were subjected to an initial basal analytical determination for uric acid, total triglycerides, total cholesterol, and uric acid clearance and fractional excretion after three days on a low purine diet,7 followed by a second determination after three weeks on a low calorie diet (1200 kcal per day: carbohydrate 50%; protein 20%; lipid 30%) with alcohol excluded. Three days after the second determinations patients were again placed on a low purine diet similar to that used before the first determination.

The Wilcoxon test was used to evaluate the significance of differences between the means in the two patient groups before and after low calorie dieting. Statistically significant differences between the two groups were calculated by the Mann-Whitney test.

The table shows the results. All the patients lost a significant amount of body weight on dieting, regardless of the group to which they belonged, but uric acid levels did not change in either group as a result of dieting.

Patients in group II (hyperuricaemic-hyperlipidaemic) exhibited considerably decreased triglyceride and cholesterol concentrations after the low calorie diet, concomitant with increased renal excretion of uric acid, which was not observed in group I.

Our results support the hypothesis that the association between triglyceride concentration and renal excretion of uric acid is more than a casual relationship, by decreasing triglyceride concentrations, we succeeded in increasing renal uric acid excretion without pharmacological intervention, while controlling the purine intake during assessment of the renal excretion of uric acid. In our opinion, the relationship is particularly valid in hyperuricaemic-hyperlipidaemic patients, as the decrease in the triglyceride concentrations and weights of the hyperuricaemia-normolipidaemic men (group I) was not accompanied by increased renal excretion of uric acid. Collantes et al6 also found that renal excretion of urate was less in hyperuricaemic-hyperlipidaemic patients than in hyperuricaemic-normolipidaemic patients. Acute increase in serum triglyceride concentrations has been shown not to modify uric acid synthesis or excretion.8 However, these data are not conclusive, as ingested triglycerides have a different composition and metabolic origin than endogenous triglycerides.

Other authors have shown an inverse correlation between insulin sensitivity and uric acid concentration,9 and between dietary caloric restriction and cholesterol and triglyceride levels from healthy volunteers.10 The potential link between the inverse relationship of the renal excretion of uric acid with hyperinsulinism and our findings remains to be determined.

The mechanisms responsible for the inverse relationship between renal excretion of uric acid and triglyceride concentrations will probably be elucidated as knowledge of the metabolic syndrome expands.

**Decreased triglyceride levels with low calorie diet and increased renal excretion of uric acid in hyperuricaemic-hyperlipidaemic patients**

**Group I**

<table>
<thead>
<tr>
<th>Uric acid (mg/dl)</th>
<th>30.1 (3.5)</th>
<th>29.8 (3.6)</th>
<th>28.7 (3.4)**</th>
<th>28.2 (3.2)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>8.3 (1.6)</td>
<td>8.4 (1.5)</td>
<td>8.0 (1.3)</td>
<td>8.0 (1.3)</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>192 (24)</td>
<td>203 (20)</td>
<td>199 (19)**</td>
<td>194 (18)**</td>
</tr>
<tr>
<td>Total triglycerides (mg/dl)</td>
<td>133 (44)</td>
<td>278 (53)**</td>
<td>90 (42)**</td>
<td>161 (51)**</td>
</tr>
<tr>
<td>Uric acid excretion (mg/24h)</td>
<td>621 (215)</td>
<td>609 (194)</td>
<td>629 (347)</td>
<td>764 (170)</td>
</tr>
<tr>
<td>Fractional excretion uric acid (%)</td>
<td>5.8 (1.4)</td>
<td>6.0 (2.5)</td>
<td>6.2 (2.5)</td>
<td>8.2 (3.2)**</td>
</tr>
</tbody>
</table>

Values are mean (SD). Group I = primary hyperuricaemic; Group II = primary hyperuricaemic-hyperlipidaemic. Significant differences: *p < 0.05, **p < 0.01, ***p < 0.001 for comparison of A with B; tpp < 0.05, tpp < 0.01, tppp < 0.001 for comparison of group I with group II.

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