Hyperuricaemia and Myocardial Infarction

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SUMMARY

The subjects of this study were 280 cases of myocardial infarction treated by the author. Hyperuricaemia correlated strongly as an associated factor. Despite lack of evidence of a casual relationship, it is suggested that possible risk factors such as hyperuricaemia be looked for and treated as a routine, so as to possibly reduce the incidence of myocardial infarction. A concept for further research is proposed.


ETYMOLOGY OF ‘GOUT’

Gutta (Latin)—drop or coagulation.
A servant of the Bishop of Chichester cured his ‘gutto’ by wearing the Bishop’s boots—13th century.
Inability to ‘go out’—James Russell Lowell, 19th century.

The incidence of myocardial infarction in South Africa remains alarmingly high. In the 3-year period 1967 - 1969 inclusive, a leading South African insurance society reported that 42% of deaths among policy holders were due to myocardial infarction. The increasing mortality and morbidity from coronary heart disease, particularly in young and middle-aged men, are also causing concern in other countries.

In a statistical bulletin issued in 1969, the Metropolitan Life Insurance Company reported mortality rates among policy holders and the general population of the USA. Ischaemic and related heart disease killed more people than all forms of cancer, all accidents and suicides together.

A recent personal study showed certain characteristics which appeared to be clearly associated with the development of myocardial infarction. One of these was hyperuricaemia. The present study was undertaken in an attempt to study further the possible significance, if any, of the relationship of hyperuricaemia to myocardial infarction.

MATERIAL AND METHODS

Two-hundred and eighty consecutive cases of acute myocardial infarction treated by myself, initially in private practice and then in the medical unit of Discoverer’s Memorial Hospital, Florida, were studied at various levels relative to possible associated high-risk characteristics. All the subjects were South African Whites. The criteria used for the diagnosis of myocardial infarction were the clinical history and examination, with ECG evidence of pathological Q waves, S-T segment changes, later T wave inversion, a falling R wave in the precordial leads, complete left bundle-branch block and, where necessary, significant and transient elevation of serum LDH and SGOT levels.

To assess levels of serum uric acid, 60 consecutive patients were investigated. A mean of 5.3 mg/100 ml (range 1.9 - 8.7 mg/100 ml) was accepted as normal for men. For females the normal mean accepted was 4.3 mg/100 ml (range 2.3 - 6.3 mg/100 ml). Blood samples were usually taken on the first Prothombin Index day (fourth day after admission) and occasionally later.

RESULTS

Serum uric acid ranged from 3.5 - 12.4 mg/100 ml (mean 6.6) for males and 3.0 - 14.0 mg/100 ml (mean 7.2) for females. Only 2 of 30 males had levels above 8.7 mg/100 ml but 25 (83%) were above the normal mean of 5.3 mg/100 ml. In the 30 females studied 19 (63%) had levels above 4.3 mg/100 ml and 26 (87%) were above the 4.3 mg/100 ml normal mean (Fig. 1).

Uric acid levels relative to age showed a remarkable similarity between males and females in the respective age groups under 60 years and those of 60 years and over. Mean values observed are shown in Table I.

Expressed in terms of means and standard error the increase in the older groups was even more obvious (Fig. 2).

The general mean for all subjects, at all ages, was 6.9 mg/100 ml (Fig. 2). More older people had levels above the mean: 36% of patients aged under 60 years, had values above 6.9 mg/100 ml, and 59% of patients aged 60 years and over, had values above 6.9 mg/100 ml. Student’s ‘t’ test was applied to the actual values and yielded the following: 58 df = 2.968; P < 0.01.

This parametric test shows a statistically significant difference between the means for age groups below and above 60 years.

Associated Gout

The incidence rates of associated gout could not be accurately assessed because several of the old patients had painful osteo-arthritis. They were not subjected to therapeutic drug challenge. However, it was quite clear that the majority of patients had never experienced clinical gout. The male patient with a uric acid level of 12.4 mg/100 ml suffered from tophaceous gout. The females with levels of 9.3, 10.9, 11.9 and 14.0 mg/100 ml had not experienced joint or musculoskeletal pains to suggest even remotely clinical gout.

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SERUM URIC ACID LEVELS IN MYOCARDIAL INFARCTION

Fig. 1. Serum uric acid levels in myocardial infarction.

**DISCUSSION**

Several authors have previously recognized an association between hyperuricaemia and atherosclerosis. Even more specifically a relationship with cerebrovascular disease and, in coronary heart disease, an increased incidence of hyperuricaemia, have also been observed.

An earlier study indicated that in myocardial infarction hyperuricaemia is one of the most commonly associated risk factors. Unanimity does not exist and some workers believe that gouty subjects are no more prone to coronary heart disease than the non-gouty. To add confusion, it has also been stated that a higher incidence of coronary heart disease in gouty subjects is real but that the association disappeared when people with clinically overt gout were removed. The results of the present series do not support this statement. A high percentage of patients had uric acid levels above the normal mean. Most of these did not suffer from clinical gout and obviously gout is but one expression of a raised serum uric acid.

Agewise, the patients above 60 years had on the average higher serum uric acid values than those below 60 years of age. Mean values for both age groups were above the accepted normal level. There were too few cases to assess a break-off point at 50 years or to detect a significant difference between the two sexes, although females actually had slightly higher levels. Sex distribution studies indicate that serum uric acid in men remains fairly constant throughout life. In females it is lower before the menopause than in men but higher after this.

Now that the association between hyperuricaemia and myocardial infarction has been shown to exist, the question must be posed whether this association is cause, effect or coincidence. The fact that over 80% of patients had serum

**TABLE I. SERUM URIC ACID LEVELS RELATIVE TO AGE AND SEX**

<table>
<thead>
<tr>
<th>Age &lt;60 years</th>
<th>Age &gt;60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>No.</td>
<td>Mean</td>
</tr>
<tr>
<td>19</td>
<td>6,1</td>
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uric acid levels above the normal mean, and the known association with atherosclerosis in the absence of acute episodes of tissue breakdown, suggests that this is not coincidental or effect. The increased levels in the older group may be related to increased formation or decreased excretion, or both.

Serum uric acid is a variable, subject to modification by a large array of complex and often interrelated factors: some brief but with others on long-term fluctuations. A few of the many factors influencing serum uric acid may be expressed in the following mnemonic:

| H | Hyperlipoproteinaemia |
| Y | Y-chromosome |
| P | Parents |
| E | Enzyme deficiencies |
| R | Reduced renal excretion |
| U | Unusual exercise |
| R | Racial |
| I | Increased nucleic acid production |
| C | Challenging tasks |
| A | Alcohol |
| E | Eating |
| M | Medicines |
| I | Inaccurate laboratory |
| A | Acute infections |

Because of this complexity of influencing and often interrelated factors, the study of significance of uric acid levels is difficult and the interpretation of associated findings is, to say the least, hazardous.

Uric acid crystals have been found in the myocardium and in myocardial infarction urate deposits have been recorded in the left ventricle adjacent to the involved coronary artery. These deposits are probably coincidental.

Increased platelet turnover with a shortened platelet survival time has been described in gout. In experimental drug studies prolongation of platelet survival time is associated with reduced platelet adhesiveness. Platelets contain serotonin or 5-hydroxytryptamine (5-HT). Injury to, or irregularity of, blood vessels may cause platelets to adhere to the vessel wall and agglutinate. Rupture of such platelets will release 5-HT which may then produce local vasoconstriction and, conceivably, intravascular thrombosis. The increased platelet turnover in hyperuricaemia may thereby be a causal factor in relation to myocardial infarction. Stress is a well known precipitating factor in acute gout. It has been suggested that challenging, eagerly accepted, stress situations relate to the development of hyperuricaemia. Stresses such as impending job loss, are certainly not challenging tasks, but they too may increase uric acid levels. Clinically there is a strong correlation between emotional stress and myocardial infarction. On the assumption that the relationship may be causal and not coincidental, or effect the concept of stress, hyperuricaemia, platelet turnover and 5-HT in coronary vessels relative to the pathogenesis of myocardial infarction may warrant further study.

Certain characteristics appear to be clearly associated with the development of myocardial infarction. Hyperuricaemia is one of the most common. The association of possible risk factors, such as stress and hyperuricaemia, does not necessarily imply a causal relationship, but until the aetiology of this apparently multifactorial disease has been clarified, it would appear reasonable to look for these factors and treat them routinely in the hope that the ultimate incidence of myocardial infarction will be reduced.

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REFERENCES