Present Status of Anticoagulant Therapy in Acute Myocardial Infarction*

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It is part of the natural history of discovery to find that enthusiasm and emotion often outstrip logic. This human failing is clearly reflected in the extravagant claims made for anticoagulants in the treatment and prophylaxis of acute myocardial infarction. Thus, despite the recommendation made for the routine use of these drugs in the acute phase of the disease, almost 15 years ago, many clinicians remain unconvinced of their value and employ these agents without enthusiasm or only on occasion. Moreover, a large segment of the medical profession today administers anticoagulant therapy in acute coronary occlusion solely to avoid criticism and the risk of legal action for malpractice.

Risk of Thromboembolism

It is true that before the anticoagulant era, when even the mildest cases were treated by immobilization in bed for six weeks or more, embolic accidents contributed to or caused a high percentage of deaths in this disease. It is also true that with the advent of anticoagulants, and the concomitant adoption of shorter periods of bed rest, greater mobility in bed and earlier ambulation, a remarkable reduction ensued in the frequency of thromboembolic complications and fatalities from this cause. In interpreting this response, however, it is well to consider that, in the same period of transition, the incidence of shoulder-hand syndrome decreased from a level of 20 per cent to a negligible frequency. Thus, if cortisone had been adopted as a routine of therapy at the same time as anticoagulants, it might be assumed today that shoulder-hand syndrome was virtually abolished by the prophylactic use of this agent. With this in mind, how much of the progress made in the reduction of thromboembolic complications can actually be ascribed to anticoagulants themselves?

To date, no studies have shown a comparison between the results of optimum management with and without anticoagulants respectively in groups of patients in whom all other variables have been meticulously controlled. In a disease in which mortality rate varies between 0 and 100 per cent depending upon the severity of the attack, the setting up of matched controls by random selection presents almost insurmountable difficulty. But, even if we accept the validity of reported findings that overall morbidity and mortality are reduced by anticoagulant therapy in acute myocardial infarction, evidence is lacking to justify its routine administration in this disease. Obviously, if the incidence of thromboembolic complications is low even without preventive measures in certain types of cases, then little can be gained from anticoagulant prophylaxis in their management. A low risk group has actually been delineated in which this conclusion appears justified. Such cases present no previous history of myocardial infarction and on initial examination reveal no evidence of intractable pain, severe or persistent shock, significant enlargement of the heart, gallop rhythm, congestive heart failure, auricular fibrillation or flutter, ventricular tachycardia or intraventricular block, diabetic acidosis or other states predisposing to thrombosis. In a series of 1000 patients designated as “good risk” on the...
basis of clinical criteria existing at the time of initial examination, the total incidence of thromboembolism under conservative therapy was only 2.3 per cent and the mortality rate, after 48 hours of observation, only 1.7 per cent (Table 1). Moreover,

<table>
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<tr>
<th>Group</th>
<th>Cases</th>
<th>Mortality Rate</th>
<th>Thromboembolism</th>
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</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>489</td>
<td>3.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Group 2</td>
<td>511</td>
<td>3.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>3.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Total</td>
<td>1,000</td>
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<td>2.3</td>
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*Percentage of deaths theoretically preventable if anticoagulants had been used.
Group 1—Retrospective study
Group 2—Prospective study

most of the complications arising in these cases were of a mild nature; cerebral embolism occurred in only one patient while embolism to an extremity was not encountered. This experience indicates that the incidence of fatal thromboembolism which is even theoretically preventable is appreciably less than 1 per cent. Thus, little potential exists for improving prognosis in such cases by means of oral agents with limited thromboprophylactic potency.

**RISK OF HEMORRHAGE**

On the other hand, if anticoagulants are used in the manner recommended for optimum protection, and not merely in token dosage, a calculated risk of at least 1 per cent mortality from hemorrhage must be accepted even in mild cases. Wright has reported 1.7 deaths per 100 cases as the human price for anticoagulant "protection" in acute myocardial infarction. In the recent Danish study, four patients out of 371 given bishydroxycoumarin (Dicumarol) orally died of hemorrhage. In addition, hemorrhagic pericardial effusion without rupture was three times as frequent in treated patients as compared with controls. Such consequences must be anticipated when benefit is sought by tampering with one of the most important and complex homeostatic mechanisms of the body. Certainly, in persons sustaining an uncomplicated first attack, it does not appear prudent to exchange the small risk of thromboembolism for the equal or greater hazard of hemorrhage.

**RATIONALE FOR PATIENT SELECTION**

Some physicians treat all patients with anticoagulants because they believe that a significant percentage of initially "good risk" cases are potentially "poor risk." Our data does not justify this position. In mild cases, if deterioration in the clinical picture does occur, it is most likely to be seen during the first 48 hours following the onset of an attack. Thromboembolism does not participate in such early change and even were this so, oral anticoagulants could have little prophylactic value during this latent phase of their activity. Although it is relatively uncommon for serious manifestations to develop after the first 48 hours of observation in "good risk" patients, the appearance of such adverse signs at any time in the course of the illness calls for the prompt injection of heparin for immediate prophylaxis. Consequently, there need be little hazard of a "good risk" patient becoming and remaining an untreated "poor risk" patient for more than a few hours. It appears illogical that those who view the sudden onset of an arrhythmia or congestive heart failure in an "unprotected" "good risk" patient as being fraught with thromboembolic danger, do not employ anticoagulants when the same arrhythmia or bout of failure arises and persists for days, weeks or months in patients without myocardial infarction. If a "good risk" patient requires anticoagulants simply because of the risk of three weeks or more of bed rest, then we should be administering these agents in patients with pneumonia, protruded disc, hip fracture, acute gout or any other condition requiring similar periods of confinement.
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Value of Anticoagulants in “Poor-Risk” Cases

In “poor risk” patients, any true benefit from oral anticoagulants probably resides in their ability to prevent venous thrombosis and pulmonary embolism. Antiprothrombin drugs have proved ineffective in averting coronary occlusion; episodes of recurrent infarction and sudden death have occurred with prothrombin levels consistently maintained in the therapeutic range. Anticoagulants have also proved ineffective in preventing cerebral and femoral thrombosis at the site of atherosclerotic lesions. Moreover, mural thrombi over infarcts have been found to form with almost equal frequency in patients on anticoagulants as in controls. These findings seriously question the prophylactic antithrombotic effect of this therapy on the arterial side of the circulation where the local release of thromboplastin from damaged intima appears to be the deciding factor in the changes leading to thrombosis. In contrast, venous thrombosis commonly results from stasis in the leg veins subjected to mechanical pressure in bed as a result of prolonged recumbency. This complication has been reduced not only by anticoagulants, but by the avoidance of over-sedation, the shortened period of bed rest, encouragement of early active and passive movement, the application of elastic bandages or stockings to the lower extremities and early ambulation. Anticoagulants appear of value in the more severe cases of acute myocardial infarction in which longer periods of bed rest are essential and circulatory disturbance contributes to venous stasis.

Long-Term Anticoagulant Therapy

If oral anticoagulants are effective in preventing venous but not arterial thrombosis, they should have little or no value when used on a long term basis to avert recurrent myocardial infarction and sudden death. The wide divergence of findings reported by competent investigators appears to support this deduction and to reflect the probable role of chance in determining the results.

Conclusion

Anticoagulants, like other drugs, should be used only under certain well-defined circumstances. In acute myocardial infarction, the initial clinical appearance of the patient, irrespective of age, constitutes the best index to his future course and the deciding factor regarding the need for anticoagulants. The physician’s knowledge of the life history of this disease and of the limitations and dangers of thromboprophylactic therapy has progressed sufficiently to warrant individual selection of cases for treatment on the basis of established clinical criteria.

References

2 Russek, H. I.: Personal Observations.