Evaluation of Anticoagulant Therapy in Congestive Heart Failure

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With the technical assistance of Mary F. Troutman, B.A.

A one year study evaluating anticoagulant drugs as an adjunct in the management of congestive heart failure has been carried out on 300 patients. Depo-Heparin and dicumarol were the drugs employed. The effect of anticoagulant therapy upon the incidence of thromboembolic complications and mortality has been studied.

The purpose of this paper is to evaluate the influence of anticoagulant therapy on the incidence of thromboembolic complications and mortality in patients with congestive heart failure. The fact that patients with congestive heart failure are prone to develop thromboembolic complications is well known. Kinsey and White\(^1\) found pulmonary infarction to be present in 24 of 50 autopsied cases of congestive heart failure. In 1947, Carlotti, Hardy, Linton and White\(^2\) noted that of 273 patients with pulmonary infarcts, the admitting diagnosis was congestive heart failure in 104.

In 1948, Anderson and Hull reported the use of dicumarol in 61 of 142 patients with congestive heart failure. Thromboembolic complications occurred in 15 per cent of the untreated group and in only 8 per cent of the patients treated with dicumarol. In 1948, Wishart and Chapman\(^3\) described the action of dicumarol therapy in 61 patients with congestive heart failure. A comparable control group was not observed. The mortality in this series was 32.8 per cent and the incidence of thromboembolic phenomena during therapy was 6.5 per cent.

The expected incidence of thromboembolic phenomena was reported to be 22 per cent.

Early in 1950, Harvey and Finch\(^4\) reported a study of dicumarol therapy in 80 of 180 patients with congestive heart failure; 100 similar patients did not receive anticoagulant treatment. Fatal thromboembolic complications, proved by autopsy, were found in 9 of the 100 control patients and in none of the dicumarol-treated group. The mortality was 17 per cent in the control group and only 9 per cent in the group receiving dicumarol. Recently, Anderson and Hull,\(^5\) in a progress report, described 297 patients with congestive heart failure, of whom 147 received dicumarol. The mortality was 13.3 per cent in the control group, and 7.5 per cent in the group treated with dicumarol.

Method of Study

During a 12 month period (July 1949 to July 1950) a study was made of the action of anticoagulant therapy in 300 patients with congestive heart failure. Shortly after admission to the medical wards of the Los Angeles County Hospital, all patients with congestive heart failure were seen by one of the authors. Initially, it was established that the patient had frank congestive heart failure. Only patients with both right and left heart failure (cardiac enlargement, basal rales, elevated venous pressure, hepatomegaly, and edema) were included. Patients with only left heart failure, acute or recent myocardial infarction, renal disease, diabetes and other major complicating illnesses were excluded.

Patients qualifying for the study were alternately placed in one of three groups. Patients in the first group were used as a control series and did not receive anticoagulant therapy. Patients in the second group received dicumarol and those in the third group, Depo-Heparin. This procedure was adhered to as rigidly as possible. The work-up and routine therapy of these patients was managed by the

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This study was aided by grants from the Los Angeles Heart Association and the Upjohn Company, Kalamazoo, Mich.

The Depo-Heparin used in this study was generously supplied by the Upjohn Company, Kalamazoo, Mich.
medical residents and house staff. The dosage and duration of anticoagulant therapy was determined by the authors. Control prothrombin and coagulation times were performed within 24 hours after hospital admission. Daily prothrombin determinations were made according to the method of Quick. Coagulation times were determined by a four tube technic, following the Lee-White method. Anti-coagulant therapy was started within 24 hours after hospital admission. It was continued until congestive heart failure was no longer present, the patient was ambulant, and soon to be discharged.

Dicumarol was administered in a dosage calculated to keep the prothrombin time between 10 and 30 per cent. Depo-Heparin sodium without vasodilators was given in a dosage calculated to keep the coagulation time between 30 and 60 minutes. It was found that 200 mg. of this type of Depo-Heparin given every 20 hours resulted in the most satisfactory prolongation of the coagulation time. This dosage was adjusted for those patients who were excessively over- or underweight.

Table 1.—Age Distribution

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Control (Group 1) (No. of Patients)</th>
<th>Dicumarol (Group 2) (No. of Patients)</th>
<th>Depo-Heparin (Group 3) (No. of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>30-39</td>
<td>1</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>40-49</td>
<td>13</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>50-59</td>
<td>23</td>
<td>22</td>
<td>16</td>
</tr>
<tr>
<td>60-69</td>
<td>39</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>70-79</td>
<td>18</td>
<td>19</td>
<td>23</td>
</tr>
<tr>
<td>80-89</td>
<td>4</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Comparison of Groups of Patients

The age distribution in the three groups has been tabulated (table 1).

In all three groups the largest number of patients were in the seventh decade, followed by the sixth, eighth and fifth decades. In respect to age distribution, the groups appear comparable.

Sex and Race. The distribution between the two sexes, and between the white and Negro races was compiled and found to be similar in the three groups.

Type of Heart Disease. Hypertensive, arteriosclerotic and rheumatic heart disease were almost the only etiologic types of heart disease present in our series of patients. The distribution of patients with these three respective types of heart disease among the three groups, while not equal, is comparable and adequate. (See table 2.)

Results

Thromboembolic Complications. In the control group of 100 patients, proved pulmonary infarction was present in 8. Three of these survived, all of whom had definite clinical and roentgenologic findings of pulmonary infarction. These 3 patients received dicumarol promptly and recurrences were not observed. In 5 of the 8 patients, the pulmonary infarcti...
In the group treated with dicumarol, 2 patients developed thromboembolic complications; one, a nonfatal pulmonary infarct and the other, a fatal cerebral embolus. Of the 7 patients in this group who died, autopsies were obtained in 2. One had rheumatic heart disease, and a cerebral embolus was found at autopsy. The other had hypertensive heart disease, and congestive heart failure was the only finding at autopsy.

**Table 4.—Autopsy Findings in Fatal Cases in the Group Receiving Depo-Heparin**

<table>
<thead>
<tr>
<th>Type of Heart Disease</th>
<th>No. of Cases</th>
<th>Cause of Death at Autopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive</td>
<td>1</td>
<td>Cerebral hemorrhage</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Congestive failure</td>
</tr>
<tr>
<td>Arteriosclerotic</td>
<td>1</td>
<td>Multiple pulmonary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>infarcts</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Congestive failure</td>
</tr>
<tr>
<td>Rheumatic</td>
<td>1</td>
<td>Multiple pulmonary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>infarcts</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Congestive failure</td>
</tr>
</tbody>
</table>

**Table 5.—Fatal Thromboembolic Complications Proven at Necropsy**

<table>
<thead>
<tr>
<th>Group</th>
<th>Deaths</th>
<th>Autopsies</th>
<th>Fatal Thromboembolic Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>18</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Dicumarol</td>
<td>7</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Depo-Heparin</td>
<td>9</td>
<td>6</td>
<td>2*</td>
</tr>
</tbody>
</table>

* Both patients developed multiple pulmonary infarcts prior to the use of Depo-Heparin.

Six autopsies were performed in the 9 fatal cases in the group treated with Depo-Heparin. Two of these patients developed multiple pulmonary infarcts prior to the onset of Depo-Heparin therapy. At autopsy, in these 2 patients, it was felt that some of the infarcts had developed after administration of Depo-Heparin had been begun. Three patients showed no thromboembolic complications at necropsy; death resulted from congestive heart failure. The patient who died of a cerebral hemorrhage during Depo-Heparin therapy had no other evidence of hemorrhage at autopsy. Shortly before death his coagulation time was 36 minutes. The autopsy findings and type of heart disease in the group receiving Depo-Heparin is tabulated in table 4.

The fatal thromboembolic complications proved at autopsy have been tabulated in table 5. Eight patients in the control group had fatal embolic complications, while only one patient in the group receiving dicumarol and 2 patients in the group receiving Depo-Heparin developed such complications.

**Discussion**

The incidence of fatal thromboembolic complications in our series has been compared with the incidence in the series reported by Harvey and Finch and Anderson and Hull. It is obvious that the results in our series and in the series of Harvey and Finch are comparable since in the two series there were respectively 8 and 9 fatal thromboembolic complications per 100 patients. In the series of Anderson and Hull, 7 out of 147 patients had fatal thromboemboli. This difference is most likely due to the decreased incidence of rheumatic heart disease among their patients as compared with those in the other two groups.

The mortality in the control group was 18 per cent, in contrast to 7 per cent in the group treated with dicumarol and 9 per cent in the group receiving Depo-Heparin (table 5). Thus the mortality among the untreated patients was twice that in either of the groups receiving anticoagulants. The reduction in mortality is due in large part to the reduction of fatal thromboembolic accidents in the patients who received anticoagulant therapy (table 5).

When our results are compared with those of Harvey and Finch, and Anderson and Hull (table 6), the results are strikingly similar. Approximately a 50 per cent reduction of mor-
Mortality was achieved in all three studies by the use of anticoagulants. This reduced mortality appeared to be the result of the lowered incidence of thromboembolic complications. In our series patients with rheumatic heart disease were particularly benefited by anticoagulant therapy.

Age distribution and mortality were correlated, and it was found that the greatest reduction in mortality was in the seventh decade where 10 deaths occurred in the untreated group. Among patients in the same decade who were treated with dicumarol and Depo-Heparin, there were one and two deaths respectively. However, the number of patients in the seventh decade in the two groups which received anticoagulant therapy was less than the number in the control group which received this therapy.

An attempt to correlate type of heart disease and mortality showed that the greatest number of deaths in the control group occurred in patients with rheumatic heart disease. An incidence of nine deaths among patients with rheumatic disease in the control group was reduced to one and 2 deaths respectively in the groups treated with dicumarol and Depo-Heparin.

Complications of Anticoagulant Therapy. There were 4 instances of bleeding among the 100 patients treated with dicumarol; epistaxis in 2, hematuria in one and melena in one. In all of these, temporary interruption of therapy resulted in a correction of the complication.

Hemorrhagic complications were found in 5 of the group receiving Depo-Heparin. There were 2 instances of ecchymoses, one of hematoma at the site of injection, one of epistaxis. In 2 of these patients the Depo-Heparin was given at 12 hour intervals instead of 20 hour intervals as ordered. The fifth patient, previously referred to, developed a fatal cerebral hemorrhage. The coagulation time in this patient was 36 minutes shortly before death; at autopsy no other evidence of hemorrhage was present.

SUMMARY
1. Three hundred patients have been studied; 100 constituted a control series, 100 received dicumarol and the remaining 100 received Depo-Heparin.
2. The incidence of fatal thromboembolic complications, proved by autopsy, was 8 per cent in the control group, 1 per cent in the group which received dicumarol, and 2 per cent in the group to which Depo-Heparin was administered.
3. The mortality was 18 per cent in the control group, 7 per cent in the group given dicumarol and 9 per cent in the group given Depo-Heparin.
4. It appears from this study that both dicumarol and Depo-Heparin are significantly effective in reducing thromboembolic complications and mortality in patients with congestive heart failure.

REFERENCES
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Circulation. 1951;4:416-419
doi: 10.1161/01.CIR.4.3.416
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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