Mitral Commissurotomy Performed During Anticoagulant Prophylaxis with Dicumarol

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Since it is possible to perform major surgical interventions on patients with lowered prothrombin-proconvertin concentration we have selected a group of patients suffering from mitral stenosis for further evaluation of this prophylactic measure. These patients are highly predisposed to thromboembolic complications. The controllable risk of hemorrhage might, therefore, be preferred to the heavy risk of thrombosis. The results of our investigations indicate a decrease in incidents of thromboembolism. No serious risk of bleeding is apparently introduced when an accurate and sensitive method of estimating the prothrombin level is used in the control of the treatment.

Patients suffering from mitral stenosis are highly predisposed to thromboembolic accidents. The major risk and most frequent cause of death during and after mitral commissurotomy is cerebral embolism. During surgery, large amounts of tissue thromboplastin enter the blood stream and in this way accelerate the intravascular coagulation. Anticoagulant prophylaxis with Dicumarol will therefore be complete only when instituted before and maintained during and after the operation.

It was shown previously that major surgical operations can be performed under effective anticoagulant prophylaxis with Dicumarol.1 The operations were successfully accomplished with this treatment at a prothrombin level in the therapeutic range, without increased bleeding or other complications.

Mitrional commissurotomy can also be performed safely under effective anticoagulant therapy with Dicumarol.2 It is the object of this paper to present and discuss the results of one year’s treatment.

Method

The level of prothrombin-proconvertin in blood was followed by an accurate one-stage assay (Owen’s method6-9). Daily determination of the prothrombin-proconvertin level was considered necessary, especially during the first several days after operation. In agreement with most authors we found the therapeutic level of prothrombin-proconvertin to be between 10 and 30 per cent. Below 5 per cent there is an increased risk of major hemorrhage, but above 10 per cent the risk is insignificant. It is essential that the determination of the prothrombin-proconvertin level be as accurate as possible. Owen’s method is very sensitive and reliable and was therefore chosen for our purpose.

Dosage: Four hundred to 500 mg. of Dicumarol were given during the first two days of treatment. The subsequent dosage was determined by the response. Individual variations often occur.8 Low prothrombin levels on the day of operation were corrected by the use of vitaminK1 (20 to 50 mg. vitamin K1, Geigy).8 Dicumarol was usually given 1 to 2 weeks preoperatively and 3 weeks postoperatively until the patient was effectively ambulatory.

Patients: The patients for Dicumarol prophylaxis were selected in the following way: Patients born on even dates received the treatment, while patients born on uneven dates received no anticoagulant prophylaxis and served as controls. However, some patients born on uneven dates and already under anticoagulant therapy were admitted to the surgical ward. This therapy had been instituted because of recent thromboembolic complication in addition to the valvular disease. We deemed the risk of new thromboembolic incidents too high if the Dicumarol therapy was discontinued, hence the prophylaxis was maintained. From Jan. 15, 1954 to Jan. 15, 1955, 26 patients

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with mitral stenosis had a commissurotomy performed under Dicumarol prophylaxis. The untreated control group of patients from the same period also consisted of 26 patients.

**Results**

*Dicumarol Prophylaxis*

On the day of operation the prothrombin per cent averaged 20; in 15 cases it was between 10 and 19 per cent, in 10 cases between 20 and 30 per cent and in one case 36 per cent. There was a slight fall in the prothrombin level in the first two or three days after the commissurotomy in 17 cases and a slight increase in four cases. A rather pronounced increase in the prothrombin level was found in five patients who received vitamin K₁ or menadion preoperatively in order to correct a too low prothrombin level. In all cases, the decrease in the prothrombin per cent was followed by a marked increase from the fifth to the seventh day and at the same time there was an increase in the maintenance dose of Dicumarol. In most cases, the daily dose of Dicumarol was 20 to 40 mg. higher in the weeks after the operation than before. In most cases, the prophylaxis was continued three weeks or more after the commissurotomy. Some of the patients were still under anticoagulant treatment when discharged from the hospital and continued this therapy as out-patients. On the whole, the treatment was stopped when the patient was as effectively mobile as before the operation. In two cases, however, the treatment was discontinued shortly after the operation. One of these patients developed severe icterus (possibly due to preoperative blood transfusions: hemolytic icterus); in the other case the treatment was stopped by mistake six days after the operation. A typical curve of the prothrombin-pro-convertin level during the period of treatment and the daily doses of dicumarol is shown in figure 1.

![Diagram](image_url)

**Fig. 1.** Mitral commissurotomy. The dosage of Dicumarol (above) and the proconvertin-prothrombin level (in per cent) in blood (below) before, during and after operation.

**Hemorrhage**

The bleeding during the operations was not measured routinely, but the postoperative loss of blood through drainage and thoracocthenesis was measured. This was compared with the loss of blood in the control group and with 50 other cases of mitral valvulotomy performed in the previous year (table 1). The loss of blood in the treated group was on an average 624 ml., in the control group, 813 ml. (In the control group there were a few difficult and complicated operations).

The average amount of blood transfused has also been compared in the two groups. The patients treated with Dicumarol received an
average of 777 ml. blood during the operation and on the days that followed. In the control group, the average amount of blood transfused was 1058 ml. (table 2). (The authors did not administer the transfusions).

These figures show clearly that the postoperative blood loss and the need of blood has not been higher for the patients under anticoagulant prophylaxis than for the patients without this therapy.

**Thromboembolic Complications**

Ten patients in the Dicumarol-treated group and 13 in the control group were above the age of 40 years. According to most reports, the risk of thromboembolic complications during surgery increases after the age of 40, so there was probably a greater risk of such complications in the control group than in the treated group.

Atrial fibrillation also predisposes to thromboembolism. Seven of the control patients and 11 of the treated patients suffered from atrial fibrillation as a complication of rheumatic heart disease. Postoperative thromboembolic incidents occurred in three of these control patients with fibrillation, while none of the 11 patients under Dicumarol prophylaxis showed signs of these complications. One of the control patients, who developed atrial fibrillation postoperatively, had a cerebral embolus. Among the patients in the treated group who developed postoperative fibrillation, no such complications occurred. In one of the patients under Dicumarol prophylaxis, a fresh atrial thrombus was found upon operating. This patient had only been treated six days preoperatively with Dicumarol, and there were no embolic complications of the commissurotomy, although she suffered from pre- and postoperative atrial fibrillation. One patient in the treated group and one in the control group had old thrombi in the atrium and an extra-auricular valvulotomy was performed. Both survived the operation without complications.

Of the 26 patients in the treated group, 7 patients had had thromboembolic incidents before surgery. No postoperative thromboembolic complications occurred among these or the other Dicumarol-treated patients in the postoperative period (3 to 4 weeks).

In the control group, four patients had had thromboembolic attacks before surgery; two of these patients developed lung infarction postoperatively.

The number of control patients with postoperative thrombotic incidents confirmed clinically was six: one died of cerebral embolism, another still has paralysis of the right arm due to cerebral embolism. Two patients recovered from cerebral embolism and two from pulmonary infarction. In addition, two other control patients suffered from probable post-

| Table 1.—Postoperative Hemorrhage after Mitral Commissurotomy |
|---------------------|-----------------|---|-----------------|
| Patients            | Average hemorrhage | Range | Distribution |
| 50 controls before Jan. 15th, 1954. | 740 ml. | 80-2160 | 10 below 480 ml. |
|                     |                 |      | 10 above 1000 ml. |
|                     |                 |      | 5 above 1060 ml. |
|                     |                 |      | 5 above 740 ml. |

| Table 2.—Amount of Blood Transfused During and After Surgery |
|---------------------|-----------------|-----------------|
| Patients            | Average amount of blood transfused | Distribution |
| 50 controls before Jan., 1954. | 835 ml. | 10 above 1500 ml. |
|                     |                 | 14 between 1000-1500 ml. |
|                     |                 | 25 between 500-1000 ml. |
|                     |                 | 1 nothing. |
| 26 controls between Jan. 1954 and Jan. 1955. | 1058 ml. | 5 above 1500 ml. |
|                     |                 | 17 between 1000-1500 ml. |
|                     |                 | 4 between 500-1000 ml. |
|                     |                 | 10 between 1000-1500 ml. |
|                     |                 | 14 between 500-1000 ml. |
operative embolism: one from a lung infarction and the other from a cerebral embolus.

**Discussion**

It is well-known that thromboembolic incidents are frequent complications of rheumatic heart disease. Recently, Bigelow\(^8\) reported 39 systemic embolic episodes in 171 patients with mitral stenosis. Seven of these patients (18 per cent) died within one month after the episode, and the rest died within three and one half years. In a survey of 393 embolic episodes in 194 patients with rheumatic heart diseases, Bland\(^9\) found the following features: Single embolic episodes occurred in 79 patients with a mortality of 30 per cent, multiple episodes occurred in 115 patients of whom 55 succeeded.

However, long-term anticoagulant therapy with Dicumarol has been shown to reduce thromboembolism in patients with mitral stenosis, atrial fibrillation and congestive heart failure.\(^10\), \(^11\), \(^12\), \(^13\)

Cerebral embolism is the most frequent cause of death after mitral commissurotomy. This was stated by Bailey\(^14\) who found 12 cases (5 per cent) of cerebral embolism in 235 patients operated on for mitral stenosis. Eight of these 12 patients died. In Bigelow’s report,\(^4\) mitral commissurotomy was performed in 88 patients. The total number of thromboembolic episodes was 17 (20 per cent of the cases) and six showed postoperative cerebral embolism (one died). In 150 patients followed-up, the total number of fatal cerebral embolism was six (4 per cent of the patients). The figures of Warren\(^15\) are also striking: 15 (16 per cent) out of 92 patients with mitral stenosis developed embolic episodes postoperatively after commissurotomy. The incidence was higher in a group of patients who previously had had embolic episodes and also in patients with atrial fibrillation. Baden\(^6\) analyzed 106 cases of mitral stenosis operated on at the University Hospital of Copenhagen. Postoperative thromboembolic complications occurred in 20 per cent. Twelve patients died after the operation and in eight of these cases, death was caused by cerebral embolism a few days after the operation.

Anticoagulant prophylaxis with Dicumarol has been used successfully after surgical operations and has reduced the frequency of thromboembolic complications.\(^17\), \(^18\) Usually this therapy has been initiated after the operation, but in some instances the first dose of Dicumarol has been administered on the evening before surgical intervention.\(^17\) Because of the lag, this prophylaxis has not been effective on the day of and the days immediately following the operation. In a previous paper, a more effective Dicumarol prophylaxis during major surgery was proposed\(^1\), \(^2\) and this prophylaxis has since been carried out in about 100 patients predisposed to thromboembolism. This treatment is begun one to two weeks prior to the operation in order to get an idea of the patient’s response to Dicumarol and to find the maintenance dose of Dicumarol. The prothrombin level on the day of operation must be above the bleeding limit (5 to 10 per cent), but must also lie in the therapeutic range. A standardized and sensitive method for the control of the therapy is therefore essential.

As most postoperative thromboembolic complications occur in the first 10 to 12 days after the operation, the anticoagulant prophylaxis should be maintained at least in this period, ideally 2 to 3 weeks and even longer in a case of atrial fibrillation.

Obviously, uncontrollable bleeding is the main risk of this procedure, but this has not occurred in this small group of patients.

Thromboembolic complications occurred among the control patients with the usual expected incidence, but none of the Dicumarol treated patients developed thrombotic diseases during the periods of treatment. Though the number of patients in the two groups is too small to allow a definite conclusion at the present time, our results as presented here have shown that an effective anticoagulant prophylaxis with Dicumarol can be maintained during mitral commissurotomy. The figures indicate that a considerable decrease in the number of postoperative thromboembolic incidents can be expected. The final evaluation of the therapy, here described, will have to wait for the treatment of a larger number of patients.
Summary

Mitrall commissurotomy was performed on 26 patients under anticoagulant prophylaxis with Dicumarol. The operations were performed with a prothrombin level in the therapeutic range (10 to 30 per cent).

Hemorrhage during and after the operations was not greater in this group of patients compared with a control group (26 patients) studied at the same time or compared with 50 similar operations performed in previous years.

Although mitral commissurotomy predisposes to thromboembolic complications, during and after surgery, this had not occurred in the Dicumarol-treated group of patients. In the control group, these complications occurred just as frequently as expected (15 to 20 per cent of the cases). A larger group of patients is necessary before the effectiveness of this treatment can be finally evaluated.

SUMMARIO IN INTERLINGUA

Commissurotomia mitral eseva executate in 26 patientes sub prophylaxe anticoagulante a Dicumarol. Le operationes eseva executate a nivellos prothrombinic intra le limites therapeutie (10 a 30 pro cento).

Hemorrhagias durante e post le operationes non eseva plus frequente in iste gruppo de patientes que in un grupo de 26 patientes de controlo qui eseva operate al mesme tempore o que in un grupo de 50 patientes subjicie a simile operationes in previe annos.

Ben que commissurotomia mitral predispone le patiente a complicaciones thromboembolic durante e post le intervention chirurgic, nulle tal complicaciones ha occurrute in le casos del patientes tractate a Dicumarol. In le gruppo de controlo le frequentia de tal complicaciones eseva de accordo con nostre expectaciones (15 a 20 pro cento). Un plus grande numero de casos debe esser observate ante que le efficacia de iste tractamento pote esser definitivemente evvaluare.

REFERENCES

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