The Effect Of The Administration Of The Anticoagulant Marcumar On The Blood Coagulation Mechanisms

Shirley A. Johnson
M. June Caldwell
Edward McCall Priest

Follow this and additional works at: https://scholarlycommons.henryford.com/hfhmedjournal
Part of the Life Sciences Commons, Medical Specialties Commons, and the Public Health Commons

Recommended Citation
THE EFFECT OF THE ADMINISTRATION OF THE
ANTICOAGULANT MARCUMAR ON THE BLOOD
COAGULATION MECHANISMS

SHIRLEY A. JOHNSON, Ph. D.*, M. JUNE CALDWELL, B.A. AND
EDWARD MCCALL PRIEST, M.D.**

The coumarin type anticoagulants are considered to decrease the plasma levels of prothrombin and of one other plasma protein related to the coagulation mechanisms, autoprothrombin I (factor VII). Autoprothrombin I is believed to drop under the influence of these drugs before the prothrombin levels begin to fall. However, the time lag between the changes of each factor varies with the anticoagulant. Recently, however, Verstraete 1954, Sise, Kimball and Adamis 1955, and Johnson and Seegers 1955, reported a decrease in the plasma levels of autoprothrombin II (Christmas factor, Plasma Thromboplastin Component) following the administration of some of these anticoagulants.

Therapeutic anticoagulant administration is controlled by the Quick one-stage prothrombin time. This test is influenced by two of the three factors which we know the anticoagulants alter, but not by all three. There is no known test that will measure changes in all three factors simultaneously with any appreciable accuracy. The Quick prothrombin time is still probably the single, most useful, test to use. Nevertheless, hemorrhage has been observed in patients with a prothrombin time reduction to only 30-40 per cent of normal according to the Quick test. This discrepancy between laboratory findings in anticoagulant control and clinical observations could be due, at least in part, to changes in plasma levels of autoprothrombin II which are not observed in the laboratory using this one routine test.

An effective anticoagulant, which does not affect the plasma levels of autoprothrombin II, might well be the safest and easiest anticoagulant to control. Marcumar is an effective anticoagulant. Control of anticoagulant effect by marcumar is noticeably smoother than with other anticoagulants. This characteristic suggested an absence of effect on autoprothrombin II and led to this present investigation.

The role of the various factors which influence the Quick prothrombin time, in thrombotic disease, has not been fully delineated. It is possible that while the levels of two factors are measured usually during anticoagulant therapy, the beneficial effect

*Department of Laboratories.
**Division of Cardiology.
of the therapy may be due to the reduction or change in the level of yet another factor. The results reported here do give us some understanding of the ease of control of one drug by the usual laboratory procedures.

METHODS

The methods used in this study have been described elsewhere, and are only briefly mentioned here.

One-stage prothrombin time: This method was described by Quick.

Two-stage prothrombin determination: Ware and Seegers described this test modified from that of Warner, Brinkhous and Smith.

Two-stage autoprothrombin I test: This test was developed by Seegers, Johnson and Penner.

Two-stage autoprothrombin II test: This test was first described by Johnson and Seegers.

RESULTS

THE PLASMA PROTHROMBIN LEVELS: In about half of the patients followed under Marcumar therapy, the two-stage prothrombin values did not change during the first twenty-four hours of therapy. However, in all ten patients the prothrombin values had dropped on the second day, and all had fallen by the fourth day to 50 u/ml. or below.

THE AUTOPROTHROMBIN II LEVELS: Unlike the anticoagulants studied previously Marcumar does not reduce the plasma and serum levels of autoprothrombin II. The cases were followed for at least fifteen days, and in some cases as long as twenty-eight days and the autoprothrombin II levels remained the same throughout. There is considerable variation in these levels before therapy. In one case, with myocardial infarction, no autoprothrombin II was found in the serum before therapy began.

THE AUTOPROTHROMBIN I LEVELS: These levels fell in the first day in every case. The fall in autoprothrombin I always preceded the fall in prothrombin or coincided with it. As has always been the case, the values for this factor were found to be higher in serum than in plasma.
DISCUSSION

Since Marcumar has been found to decrease the plasma levels of autoprothrombin I and prothrombin, but not autoprothrombin II, the significance of this latter component in the treatment of thrombosis can be considered. It is known that autoprothrombin II is deficient in patients with hemophilia B\textsuperscript{10,11}. One of our patients sustained a myocardial infarction in the face of an absence of autoprothrombin II. There was no history of hemorrhagic tendency in this case. The anticoagulants Dicumarol, Hedulin, Tromexan and Sintrom all may reduce the autoprothrombin II level to practically zero without patient hemorrhage\textsuperscript{12}. Conversely, patients may hemorrhage when the determined prothrombin time is not sufficiently reduced to account for this, and it has been postulated that a reduction of autoprothrombin II may be the explanation for this undesirable effect. Marcumar produces a reasonably stable anticoagulant effect as measured by the Quick prothrombin time. This observation is enhanced by clinical experience\textsuperscript{13}. Numerous reports attest to Marcumar as an effective anticoagulant\textsuperscript{14,15,16}. Since autoprothrombin II is not reduced by this drug, it is possible that its reduction is not necessary for effective anticoagulation therapy.

There is another consideration to bear in mind. It has been suggested by O'Brien that autoprothrombin II may have a prosthetic group which is phospholipid in nature\textsuperscript{17}. This offers a possible connection between the lipids of blood and the coagulant mechanisms in the problem of thrombosis. The part played by this factor autoprothrombin II on the thrombosing tendency is very obscure and difficult to evaluate. Considerably more time will need to elapse, in all probability, before the study is complete.

CONCLUSIONS

The changes in the plasma levels of the pertinent components in the blood coagulation mechanisms have been studied in conjunction with the administration of the anticoagulant, Marcumar. This drug, Marcumar, does not alter the plasma levels of autoprothrombin II (PTC, Christmas factor) as does Dicumarol, Tromexan, Hedulin or Sintrom. The findings may account for the observation that anticoagulant therapy can be easily controlled with Marcumar as the Quick prothrombin time is the commonly used laboratory test under these circumstances, and this test is not influenced by different levels of autoprothrombin II. The concepts involving autoprothrombin II in the formation of intravascular thrombosis are viewed.

BIBLIOGRAPHY


